DISEASES of the CHEST

VOLUME XXXVIII OCTOBER, 1960 NUMBER 4

Stereoscopic Study of the Inflated Lung*

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Stereomicroscopic study of the inflated pulmonary parenchyma offers a three-dimensional approach to the structure, vascular details and cellularity of lungs. The gross characteristics and the interrelationships of the parenchymal structures are more clearly observed. Preliminary observations on the unstained alveolar and pleural aspects of the lungs were documented by Joannides,[1] whose observations did not differ greatly from the concept obtained by Miller[2] following reconstructional studies.

Inflation and drying of fresh lungs is nothing new, and has been used primarily to provide museum specimens for instructional purposes. In an effort to simulate the in vivo structure of the lung, other investigators have used Woods metal, colored gelatin, formaldehyde, Kaiserling solution and liquid latex.[3,4] All of these methods have been employed to demonstrate primarily one facet of the pulmonary parenchyma, such as the vascular bed, the bronchiolar structure, or the alveolar membrane.

In our studies, we have combined the efforts of many previous investigators, using stereomicroscopic studies of serial sections of inflated lungs, both unstained and specifically stained sections. At first, the three-dimensional view of pulmonary parenchyma, either stained or unstained, seems

*Presented at the Homecoming Meeting, American College of Chest Physicians, October, 1959, Albuquerque, New Mexico.
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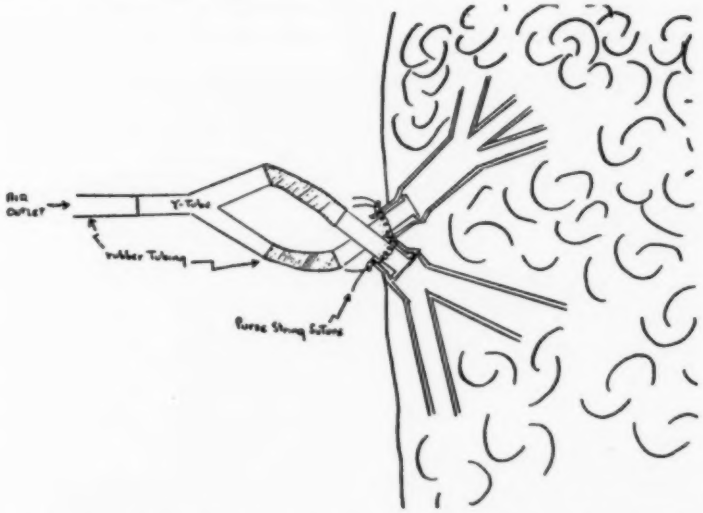

FIGURE 1: Flared ends of medicine droppers in upper and lower lobe bronchii with purse string suture in place.

to present a bizarre, sponge-like structure. With further study, one is presented with a concept of coordinated structures that opens up new vistas in the field of normal configuration and pathologic change. The material accepts almost all biological stains, and the method of plastic impregnation facilitates handling and shipment to other observers without distortion of the tissues or possibility of breakage. Stereomicroscopic serial section study may provide a more concise understanding of various disease processes that affect the lungs, for example, emphysema and bronchitis. Boren and Blumenthal[3] have aptly demonstrated in their preliminary studies that these stained sections provide a greater understanding of the component portions of the pulmonary parenchyma.

Lungs or lobes, obtained from necropsy or surgery, may be prepared either in the fresh state or placed in the deep freeze for processing at a convenient time. The frozen lungs demonstrate satisfactory inflation of the parenchyma after five months in the deep freeze. It is noteworthy to state that frozen lungs should be thawed gradually in lukewarm water or else left at room temperature with a moistened towel over the pleura to prevent drying and cracking.

The preparation of material for fume inflation necessitates a preliminary careful observation for pleural tears. These can be controlled by small ligatures, using size O black silk. The pulmonary artery is tightly sutured and the veins left open to provide drainage of residual blood in the lungs. Boren has also sutured the veins in order to provide prominence of the vascular system. In our hands, this procedure of venous closure increases the brittle state of the tissue and causes excess fragmentation when the lungs are being cut.

The bronchial stump is cannulized, using the flared end of medicine droppers for the upper and lower lobes (Fig. 1). A purse string suture is passed through the secondary carina, anchoring each cannula separately in place. The lower lobe cannula should not be placed too deeply in order to avoid obstruction of the right middle lobe bronchus, and

FIGURE 2: Inflated lung with fissure approximation.

similar care should be taken not to obstruct the lingular bronchus on the left. The use of two cannulae with the Y tube allows individuual adjustment of flow to the upper and lower lobes. Y tube connections are placed to both cannulae and the lung is ready for inflation which should begin gradually until the specimen is completely expanded. We have been using the criterion of fissure approximation as an indication of an expanded lung within the thoracic space. When the fissures are approximated, the air flow is adjusted so that the lung maintains this state without further pressure variations (Fig. 2). The specimen is maintained on the manifold system for a minimum of seven days. A shorter period of time will invariably result in shrinkage and distortion after the lungs have been removed from the inflation apparatus.

The inflation manifold (Fig. 3) is constructed of copper tubing with valves and outlets into containers for formaldehyde, drying agent, and 95 per cent alcohol. The compressed air is passed over the solutions, utilizing the Venturi principle, in order to saturate the air volume with fume, rather than liquid material. The air dessicant is interspersed between the formaldehyde solution and the alcohol mixture in order to avoid transport of formaldehyde droplets into the lung. The formaldehyde and alcohol fumes serve to fix the lung in the inflated state as well as preserve some of the natural coloration of the tissue. A small quantity of glacial acetic acid added to the alcohol mixture will enhance nuclear staining techniques. It is probably best not to exceed pressures of 20 to 30 cm. of water passing through the manifold into the lung. Of utmost importance is a compressor with adequate output and reserve. A pressure reducing valve inserted between the compressor and the manifold will avoid excess surges of compressed air with possible rupture of pulmonary tissue. Such reducing valve also allows the use of increased flow of air through the manifold without increasing the pressure excessively.

The lungs are sectioned by using a scalloped meat cutting blade on a conventional band saw. For our purposes, we devised a carriage con-

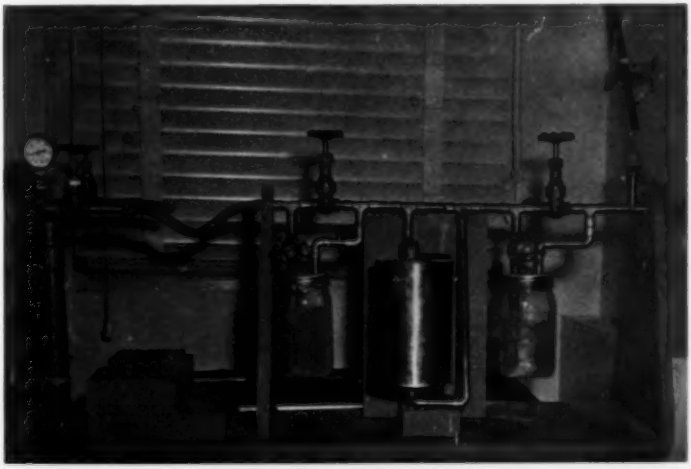

FIGURE 3: Inflation manifold left to right, formaldehyde solution, drying compound, and alcohol mixture.

nected to a screw type band saw "gate" which permits sections as thin as one millimeter. In order to study interalveolar relationships, we sectioned most of our material in 2 mm. slices. Although the tissue can be manually held in the carriage, we cemented one end of the lung to the side of the band saw gate, in order to obtain consistent serial sections without endangering the fingers of the operator (Fig. 4).

The staining procedures follow standard histologic techniques plus the fact that all phases must be accomplished under vacuum. This provides for a thorough staining of these sections which are considerably thicker than the standard 5 mμ specimen. Constant observation is necessary to prevent overstaining or under differentiation. The method of plastic impregnation is best accomplished in a vacuum oven. At present, we believe that the easiest and safest to work with are the apoxy resins. For routine study, the stained sections may also be mounted in "Permount."

The stereoscopic study of pulmonary parenchyma prepared and stained as described above provides the observer with a more comprehensive understanding of pulmonary anatomy, histology, and pathology (Fig. 5). Single plane observations made with the conventional microscope do not easily permit a continuous study of all adjacent areas, above and below the focal plane being studied. Extension of disease to adjacent areas can be observed more readily, especially in such instances as pulmonary emphysema. The variations in the degenerative processes involving pulmonary parenchyma can be studied in contiguous levels of tissue without resorting to the tedious study of single plane serial sections. With the application of histochemical staining techniques, it is possible to observe the normal and abnormal course of the alveolar capillary bed, pigment aggregates, depositions of fibrous tissue and other evidences of alveolar degenerative involvement. Bronchial and broncho-alveolar structures

FIGURE 4: Lung being sectioned with band saw.

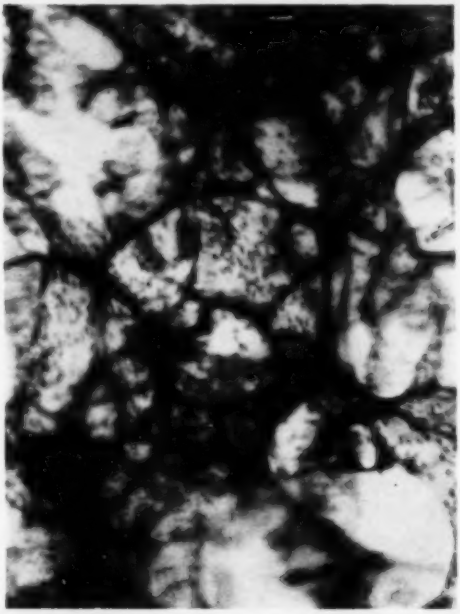

FIGURE 5: Stereoscopic photomicrogram of pulmonary parenchyma.

with the major ramifications can be observed more clearly and perhaps provide a better understanding of pulmonary ventilation. The stereoscopic observations of pulmonary parenchyma in general provide a three-dimensional aspect which is more comprehensive than conventional microscopy and assists in better understanding of the normal and diseased structure.

SUMMARY

A method for inflation of pulmonary parenchyma is described which, combined with histochemical staining and stereoscopic study, may shed more light on our present concept of the anatomy, pathology, and physiology of the lungs.

RESUMEN

Se describe aquí un método para inflar el parénquima pulmonar, el que combinado con la coloración histoquímica y el estudio estereoscópico, puede proporcionar cierta luz sobre nuestro concepto actual de la anatomía, la patología y la fisiología pulmonar.

RESUMÉ

Les auteurs décrivent une méthode d'insufflation du parenchyme pulmonaire qui, associée à une coloration histochimique et une étude stéréoscopique, peut apporter davantage de lumière sur notre conception actuelle de l'anatomie, de la pathologie et de la physiologie des poumons.

ZUSAMMENFASSUNG

Beschreibung einer Methode zur Aufblähung von Lungenparenchym. Sie vermag in Verbindung mit histochemischer Färbung und stereoskopischer Untersuchung mehr Licht auf unsere derzeitige Auffassung von Anatomie, Pathologie und Physiologie der Lungen zu werfen.

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Thoracic Surgery in Mentally Ill Patients

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General Observations

Adequate care of mentally ill patients presenting pulmonary disease (non-specific infections, lung abscesses, bronchiectases, empyema), malignant and benign tumors and the demands of an effective tuberculosis control program necessitate the application of thoracic surgery in hospitals for the mentally ill. It is worthy of note that the incidence of tuberculosis detected among patients admitted to the Illinois Department of Public Welfare's 13 mental hospitals and the two schools for the mentally retarded is 29 times greater than the reported incidence in the general population.[1] These institutions have an average total resident patient population of about 48,000.

To serve this institutional system, thoracic surgical centers were set up at Kankakee State Hospital in 1951 and at Chicago State Hospital in 1954. A thoracic surgical service established in 1957 provides consultation and surgical service to all state welfare institutions.

Under the present program, conferences at which the medical, surgical and roentgen departments are represented, screen the patients and on recommendation they are channeled to either of the two centers for final evaluation and treatment.

The following is a report on the major thoracic surgery performed on mentally ill or retarded patients under the department's auspices and at the Veterans Administration Hospital, Downey, Illinois, a 2,847-bed neuropsychiatric facility. The period covered is from October, 1947 through December, 1957, with follow-up ranging from one to eleven years.

During this period there were 388 procedures performed on 343 patients with an overall post-operative mortality (within 90 days) of 23 patients (6.7 per cent). Eighty-six of these procedures were conducted at the Veterans Administration Hospital.

These patients represent a cross-section of the various types of mental disease, including schizophrenics, chronic alcoholics with deterioration and senile dementias, epileptics and mentally retarded with and without psychosis. It must be emphasized that we are dealing surgically with the chronic mentally ill patient. An insight into the reluctance of the relative and a tactful approach to this problem are very necessary.

For analytical purposes, the patients are divided into tuberculous and non-tuberculous categories. Many were not optimal risk candidates for surgery.

Tuberculous

There were 295 procedures performed on 251 tuberculous patients. Only four procedures were performed during the period from October,

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1947 to January, 1950. There were 195 men (78 per cent) and 56 women (22 per cent). One hundred and four patients (41.4 per cent) were in the age group above 50 years.

Table 2 lists the extent of disease showing 12.4 per cent had minimal, 54 per cent moderately advanced and 35.6 per cent far-advanced pulmonary tuberculosis. Bilateral involvement was present in 70.9 per cent and positive gastric or bronchoscopic cultures were obtained in 104 (41.4 per cent) (Table 3). Pulmonary involvement varied from the asymptomatic solitary circumscribed nodule to the totally destroyed lung. A small group of these were resistant to anti-tuberculosis medical therapy, having been treated for three to four years without conversion. This prolonged therapy was often due to difficulty in obtaining permission for surgery from the guardian or nearest relative.

Table 4 lists the type of surgery. Five patients had bilateral surgery, three having bilateral resections and two bilateral thoracoplasties with subscapular paraffin pack. Eighty-six thoracoplasties, conventional or with plombage, were performed as primary procedures; 25 conventional thoracoplasties were done as secondary procedures to obliterate dead space or empyema. One hundred and seventy eight (60.3 per cent) patients underwent resectional surgery.

The majority received three anti-tuberculous drugs (streptomycin, INH and PAS) or combination of two of these. Patients having resistant organisms prior to surgery were given viomycin sulfate. Following surgery, patients routinely received two years of chemotherapy.*

Results:

Forty-five (17.9 per cent) patients were discharged as cured of their mental illness. Forty had inactive pulmonary disease and five were transferred to sanatoria for further treatment of tuberculosis. Table 3 gives the pre- and post-operative bacteriological status of 237 patients. The post-operative deaths (within 90 days) were not evaluated post-surgically relative to their bacteriological status. Two hundred and seven (82 per cent) are negative after surgery. Of these, 127 (50.6 per cent) have had anti-microbial therapy discontinued for one to five years and they are considered inactive both radiologically and bacteriologically. Eighty patients are negative, but are still on chemotherapy consistent with the policy of giving anti-tuberculosis therapy for two years post-operatively. Thirty patients with bilateral disease are still active bacteriologically and are receiving chemotherapy.

Complications:

One hundred and seventy-two (68.5 per cent) had no complication. The remaining had one or more complications, and these are listed in Table 5.

Atelectasis: As recorded in a preliminary report[3] as well as others,[3,4] atelectasis was the major complication. This occurred after 55 procedures: 48 (26.9 per cent) post-resection and seven (6 per cent) post-thoracoplasty. There were two post-operative deaths due to this complication alone and two others in which it was a contributory cause (see: mortality). The cause of the atelectasis was the refusal or inability of

patients to cough. It is necessary to follow such patients closely and initiate active measures as soon as the diagnosis of early atelectasis is made. At one of our institutions, a supplementary tracheotomy is done routinely on patients who are not expected to cooperate well in the immediate post-operative period. This has reduced the incidence of this complication in that institution.

Bronchopleural fistula: Twenty-six (14.6 per cent) patients developed fistula after resection. Sixteen were positive for acid-fast bacilli prior to surgery. Twenty-two were men and four women. Eight of these resulted in post-operative deaths and were complicated by empyema in five, contralateral spread in one and atelectasis in two. One died 17 months after surgery of bronchopleural fistula and empyema. Thirteen (50 per cent) were controlled with thoracoplasty or tube drainage and suction. Three fistulae have not closed after collapse measures. One patient was transferred to a tuberculosis sanatorium with an open fistula.

Mortality:

There was an overall mortality of 34 (13.5 per cent) from all causes with an operative mortality (within 90 days) of 14 (5.6 per cent). Of the latter, one post-operative death occurred from hemorrhage in the operating room. The others followed secondary surgery performed to control bronchopleural fistula following resection. Seven of the 14 post-operative deaths were in the age group above 50 years.

The following lists the causes of death:

Death in operating Room		— 1	} 14 (5.6 per cent)
Hemorrhage	—1		
Post-operative deaths within 90 days		—13	
Emphyema and B-P fistula	—5		
B-P fistula and contralateral spread	—1		
B-P fistula and atelectasis	—2		
Atelectasis	—2		
Pulmonary embolus	—2		
Extraneous:			
Asiatic flu	—1		
Three months to a year		—3	
Spontaneous pneumothorax and contralateral spread			—1
Spread of disease and empyema			—1
Extraneous:			
Hip fracture and hypostatic pneumonia			—1
One to two years		—6	
Spread of disease			—1
Bronchopleural fistula and empyema			—1
Extraneous:			
Hip fracture and hypostatic pneumonia			—1
CA of the pancreas			—1
CA of the stomach			—1
CVA and diabetes			—1
Two to four years		—8	
Spread of disease			—1
Extraneous:			
Bronchopneumonia			—3
Perforated duodenal ulcer			—1
CA of the tongue			—1
Chronic myocardial insufficiency			—1
Suicide			—1
Four to 11 years		—3	
Extraneous:			
Coronary thrombosis			—1
Bronchopneumonia			—1
Pulmonary edema and cor pulmonale			—1

TABLE 1 — GENERAL INFORMATION

		TB	NON TB
Number of patients	343	251	92
Number of procedures	388	295	93

SEX

TB (Men	195 — 78 per cent	NON TB (Men	55 — 59.8 per cent
TB (Women	56 — 22 per cent	NON TB (Women	37 — 40.2 per cent

AGE DISTRIBUTION BY DECADES

	MEN		WOMEN	
AGE	TB	NON TB	TB	NON TB
10 - 19	1	1	0	0
20 - 29	12	1	2	4
30 - 39	53	2	12	1
40 - 49	54	14	13	12
50 - 59	50	10	23	14
60 - 69	23	24	5	6
70 - 79	2	2	1	1

Average (TB 46.3 years; Non TB 58.4 years)

Non-Tuberculous

Ninety-three procedures were performed on 92 patients. Fifty-five (59.8 per cent) were men and thirty-seven (40.2 per cent) were women. The ages ranged from 17 to 78 years with an average of 58.4 years (Table 1). Fifty-three (57.6 per cent) were over the age of 50 years. Of these there were 38 men and 15 women.

Table 2 lists the type of surgery. There were 53 pulmonary resections, of which 14 were for lung abscess, eight for bronchiectasis, two for cystic lung and bullae, five for non-specific granulomas and one for hamartoma. One secondary thoracoplasty was performed to control a bronchopleural fistula. Exploratory thoracotomy was performed on 30 patients for bronchogenic carcinoma and four for metastitic carcinoma. Twenty-three of these were resected, and the remaining eleven were inoperable. Eight patients had carcinoma of the esophagus, four of these had esophageal resection with gastro-esophageal anastomosis. In the remaining four, esophagotomy with insertion of an indwelling plastic tube was performed as a palliative procedure for obstruction. Twenty other surgical procedures were performed for excision of mediastinal tumors or cysts, or removal of intra-thoracic foreign bodies.

Complications:

Thirty-two (35.8 per cent) patients had complications. The most common complication was atelectasis occurring in 24.3 per cent. There were five with post-operative cardiac irregularities occurring in the older age group. Two had bronchopleural fistulae, one after segmental resection

TABLE 2 — EXTENT OF DISEASE

	Per cent	Unilateral	Bilateral
Minimal	12.4	31	0
Moderately Advanced	54	42	93
Far Advanced	35.6	0	85

for lung abscess and the other after lobectomy for bronchogenic carcinoma. The former was controlled by a tailoring thoracoplasty, the latter developed empyema with atelectasis and bronchopneumonia on the opposite side and expired. One, a mental defective, had difficulty in swallowing after pulmonary resection with routine post-operative tracheotomy. He had complete anesthesia of the pharynx, larynx and trachea and absence of cough reflex without paralysis of the vocal cords. Tracheobronchial toilet was maintained through the tracheotomy and by bronchoscopy without anesthesia. Eventually he regained full control of deglutition. The possibility of this being a hysterical conversion symptom must be considered.

Mortality:

The overall mortality from all causes was 30 (32.6 per cent) with an operative mortality (within 90 days) of nine (9.8 per cent). Twenty-four of the 30 patients who expired were in the age group above 50 years. Seventeen died from the progression of bronchogenic carcinoma. Five of these were resected; the remaining were considered inoperable. Three died from pulmonary edema, two in the immediate post-operative stage after pneumonectomy. Eight expired from progression of carcinoma of the esophagus. Four of these were resected and four had palliative procedures.

The following lists the causes of death:

Post-operative deaths (within 90 days) — 9 (9.8 per cent)
- Pulmonary edema — 2
- Progression of bronchogenic carcinoma with metastases — 5
- Bronchopleural fistula, empyema, atelectasis, left, bronchopneumonia, right — 1
- Progression of cracinoma of the esophagus with metastases — 1

Three months to a year — 11
- Spread of bronchogenic carcinoma with metastases — 3
- Progression of carcinoma of the esophagus with metastases —5
- Bronchopneumonia — 1
- Pulmonary edema and atelectasis — 1
- Septecemia, secondary to pyelonephritis — 1

One to two years — 6
- Spread of bronchogenic carcinoma with metastases — 2
- Spread of carcinoma of the esophagus with metastases — 2
- Status epilepticus — 2

Two to four years — 4
- Spread of bronchogenic carcinoma with metastases — 3
- Acute coronary occlusion — 1

Four to 11 years — none

Psychiatric Aspects

Modern psychiatric treatment permits the acutely ill psychotic to leave the institution early and return to productive work. Chronically ill psychotics also have undergone a change. Though in need of prolonged

TABLE 3 — PRE- AND POST-OPERATIVE BACTERIOLOGICAL STATUS*

	On CCT	Off CCT**
Positive Before Surgery, Negative After	31	58
Negative Before Surgery, Negative After	49	69
Positive Before Surgery, Positive After	27	0
Negative Before Surgery, Positive After	3	0

*Excluding post-operative deaths.
**Combined chemotherapy.

institutional care, they are more cooperative, approachable and amenable to treatment of physical illnesses.[5] The present goal is to permit these patients to lead as near a normal life as possible within the institution and to prepare them for discharge.

Close and frequent contact with the patients in their daily routine is important for obtaining satisfactory post-surgical cooperation. Many patients become suspicious and aggressive if approached by someone unknown to them. The mental outlook of the patients has an important bearing on post-operative recovery. Patients who use their pulmonary condition as an escape or crutch to justify their mental aberration resist efforts towards improvement. A majority of our patients are on some form of ataractic therapy, a few on fairly large doses. This is usually discontinued about two or thee days prior to surgery to avoid any potentiating effect of the anesthetic. Post-operatively, some patients are re-started on small doses of the ataractics.

Certain difficulties have arisen peculiar to the treatment of mentally ill or retarded patients.[5] In the case of pulmonary tuberculosis patients, the problem of collecting good sputum specimens, due to the patients' unwillingness or inability to cooperate, necessitates doing gastric lavages. The administration of drugs occasionally imposes a problem. Some patients refuse medication orally and others parenterally. In the tubercu-

TABLE 4 — TYPES OF SURGERY

	TB	NON TB
Resections Total	178	53
Wedge	39	8
Segment	50	10
Lobectomy	71	28
Pneumonectomy	13	7
Pleural pneumonectomy	1	0
Decortication	4	0
Thoracoplasties Total	111	1
Thoracoplastry with plombage	64	
Thoracoplastry — conventional (primary)	22	
(secondary)	25	1
Esophageal resection		4
Esophagotomy and insertion of tubes		4
Others	3	20
Exploratory thoracotomy and biopsy	3	11
NON TB PATHOLOGY		
Bronchiectasis	8	
Lung abscess	14	
Cystic lung and bulla	2	
Bronchogenic carcinoma — resected	19	
— biopsied	11	
Metastatic carcinoma	4	
Osteochondroma rib	1	
Mediastinal tumors and cysts	7	
Intra-thoracic neuroma	2	
Carcinoma esophagus	8	
Intra-thoracic foreign bodies	5	
Pericardial cysts	5	
Granulomas	5	
Hamartomas	1	

TABLE 5 — COMPLICATIONS

	TB	NON TB
Pulled out tube	7	4
Abdominal distention (ileus)	4	3
Atelectasis	55	18
Pulmonary edema	2	2
Hemorrhage and shock	1	
Loss of swallowing reflex		1
Wound infection	4	1
B-P fistula	26	2
Spread to opposite side	9	
Massive subcutaneous emphysema	3	0
Empyema	9	1
Cardiac arrhythmias	6	5
Unexpected lung	10	1
Bacteremia	1	
Number of patients without complications	171	60

losis patients the combination of anti-tuberculous drugs is often modified to avoid undue stress to the patients. It is mainly in this group that drug therapy has been intermittent and varied.

Consent for surgery in the incompetent patients must be obtained from the guardian or nearest relative. This at times has been difficult to obtain.

SUMMARY

Analysis of the 388 procedures performed on 343 tuberculous and non-tuberculous mentally ill patients reveals a post-operative mortality of 23 (6.7 per cent). The overall percentage of post-operative mortality for tuberculous patients was 5.6 per cent. The latter mortality, however, occurred only after excisional surgery and represents a rate of 7.9 per cent for resections, which compares favorably with those performed on non-mental patients.[6,7] The operative mortality in the non-tuberculous patients was greater, due to early death from progression of the malignant process. One hundred and fifty-seven (45.8 per cent) of these patients were over the age of 50 years and 15 (65.2 per cent) of the post-operative mortality were in this age group.

Atelectasis occurred after 73 (18.8 per cent) of the procedures. Post-operatively patients must be closely observed and active measures initiated before massive atelectasis occurs. This is especially true of the severe mental deficients and the chronic psychotic patients who are passively cooperative prior to surgery and refuse or are unable to follow instructions in the post-operative phase, occasionally becoming catatonic.

Among the patients with pulmonary tuberculosis, good results were obtained in 82 per cent. Eight patients are still on chemotherapy and are negative.

RESUMEN

El estudio de 388 procedimientos quirúrgicos llevados a cabo en 343 enfermos mentales tuberculosos y no tuberculosos, reveló una mortalidad de 23 (6.7 por ciento). (El porcentaje de mortalidad posoperatoria para los tuberculosos, fué de 5.6). Esta mortalidad ocurrió después de cirugía de excisión y representa una proporción de 7.9 por ciento para las resecciones, la que se compara favorablemente con la obtenida en casos no mentales de 5.6. La mortalidad operatoria de los enfermos no tuberculosos fué mayor debida a muerte temprana por progreso de padecimiento maligno. Ciento cincuenta y siete (45.8 por ciento) de estos enfermos eran mayores de 50 años y 15 (65.2 por ciento) de la mortalidad posoperatoria fué en este grupo de edad.

La atelectasia ocurrió después de 73 (18.8 por ciento) de las operaciones. Los enfermos deben ser observados cuidadosamente en el postoperatorio y deben llevarse a cabo medidas activas antes de que se presente la atelectasia voluminosa. Esto es cierto en especial en los mentales severamente afectados por deficiencia y en los psicóticos crónicos que son pasivos en su cooperación antes de las operaciones y rehusan seguir las instrucciones en el postoperatorio volviéndose en algunos casos catatónicos.

Entre los enfermos con tuberculosis pulmonar, se obtuvieron buenos resultados en 82 por ciento. Ochenta enfermos están aún bajo quimioterapia y son negativos.

RESUMÉ

Une analyse de 388 interventions pratiquées sur 343 malades mentaux tuberculeux et non tuberculeux révèle une mortalité post-opératoire de 23 cas (6.7%) (Le pour-

centage de mortalité post-opératoire des malades tuberculeux a été de 5.6%). Ce dernier taux survint après chirurgie d'exérèse et repràsente un taux de 7.9% pour les résections, qui se compare favorablement avec ceux pratiqués sur les malades non mentaux. La mortalité opératoire chez les malades non tuberculeux fut plut importante, imputable à la mort précoce par évolution de processus malins. 157 (45.8%) de ces malades avaient dépassé l'âge de 50 ans, et 15 (65.2%) de la mortalité post-opératoire appartenait à ce groupe d'âge.

Une atélectasie survint après 73 de ces interventions (18.8%). Les opérés doivent être étroitement observés, et d'actives mesures prises avant qu'une atélectasie massive ne survienne. Ceci est particulièrement vrai chez les déficients mentaux, et les psychopathes chroniques qui n'ont manifesté aucune coopération active avant l'opération et refusent de suivre les instructions qu'on leur donne dans la phase post-opératoire, devenant éventuellement catatoniques.

Chez les malades ateints de tuberculose pulmonaire, de bons résultats furent obtenus chez 82%. 80 malades sont encore sous chimiothérapie et ont une expectoration négative.

ZUSAMMENFASSUNG

Eine Auswertung von 388 Eingriffen, die an 343 tuberkulösen und nichttuberkulösen Geisteskranken vorgenommen worden waren, ergab eine postoperative Mortalität von 23 (6,7%) (der Prozentsatz für die postoperative Mortalität für tuberkulöse Patienten betrug 5,6%.). Die Sterblichkeit für letztere betraf Exzisionen und bedeutet eine Zahl von 7,9% für Resektionen, die sich gut vergleichen läßt mit derjenigen für nicht geisteskranke Patienten (5,6%). Die operative Mortalität bei den nichttuberkulösen Patienten war größer und zwar als Folge früher Todesfälle durch Progredienz des malignen Prozesses. 157 (45,8%) dieser Kranken waren älter als 50 Jahre, und 15 postoperative Todesfälle (65,2%) lagen in dieser Altersgruppe.

Zu einer Atelektase kam es nach 73 (18,8%) der Eingriffe. Die Patienten müssen unmittelbar nach der Operation sorgfältig beobachtet und aktive Maßnahmen eingeleitet werden, ehe eine massive Atelektase eintritt. Dies trifft in besonderem Maße zu bei schweren Fällen von Geisteskrankheiten und chronischen Psychosen, die schon vor der Operation wenig zugänglich sind und sich in der postoperativen Phase weigern, irgendwelche Instruktionen zu befolgen und sogar gelegentlich katatonisch werden.

Bei den Kranken mit Lungentuberkulose erzielte man gute Resultate in 82%. 80 Patienten werden noch mit Chemotherapie behandelt und sind negativ.

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A Comparison of Various Segments of the Forced Expirogram with the Maximum Breathing Capacity*

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Introduction

There are a number of factors which influence the maximum breathing capacity. Among these are muscle strength, neuromuscular co-ordination, compliance and elasticity of the lungs and soft tissues, and airway resistance, as well as size, age and sex.

Since the introduction of the concept of timed vital capacity in 1951,[1] various portions of the forced expirogram have been suggested as useful for indicating the presence of increased airway resistance.[1-3] A correlation between the maximum breathing capacity and portions of the expirogram has also been demonstrated.

The purpose of this study was threefold; 1) to determine which portion of the forced expirogram was best correlated with the maximum breathing capacity; 2) which portion gave the highest degree of discrimination between widely different levels of maximum breathing capacity, and 3) the relative merits of the various segments of the forced expirogram as a screening tool.

Materials and Methods

Five hundred men were studied; most of whom were coalminers, many with some degree of pulmonary emphysema. Hospital employees and physicians were also included. The maximum breathing capacity of the subjects varied from 12 to 230 liters per minute.

The Godart-Pulmotest double spirometer system† was used. The maximum breathing capacity was determined over a period of 12 to 15 seconds; only those individuals who cooperated sufficiently to give less than 5 per cent variation on repeat testing were included in the study. The expirograms were done in at least triplicate with a kymograph paper speed of 1200 millimeters per minute. The forced expirogram which was expelled at the most rapid rate was used for the various measurements. Patients with technically unsatisfactory records, or those lacking repeat reliability, were excluded from the study. It should be noted that repeat reliability is more often obtained in the diseased patient, the malingerer or the neurotic by means of the forced expirogram than is repeat reliability of the maximum breathing capacity.

Twelve different portions of the expirograms were measured. Six different timed vital capacities were measured; these are expressed as a percentage of the total vital capacity. The subscript refers to the time over which this percentage was measured (TVC_t). Six forced expiratory flow rates were measured, the results are expressed as cubic centimeters

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†Obtained from Instrumentation Associates, New York, New York.

per seceond. The subscript refers to the time interval over which the flow rate was measured ($FEFR_t$). The various portions were analyzed and plotted against the maximum breathing capacity in liters per minute (Figures 2 to 5): ½ second timed vital capacity ($TVC_{0.5\ sec.}$), ¾ second timed vital capacity ($TVC_{0.75\ sec.}$),[2] 1 second timed vital capacity ($TVC_{1.0\ sec.}$), 2 second timed vital capacity ($TVC_{2.0\ sec.}$), 3 second timed vital capacity ($TVC_{3.0\ sec.}$);[11] a delayed 1½ second timed vital capacity, which is obtained by discarding the first 300 cc's of the forced expirogram and measuring the percentage of the total forced vital capacity expelled over the subsequent 1½ second, ($TVC_{-300,\ 1.5\ sec.}$); the maximum flow rate[3] measured for the most rapid 600 cc's ($FEFR_{max.\ 600}$), the mid-exipratory flow rate[4] ($FEFR_{25\ to\ 75\ per\ cent}$), the flow rate over the last half of the mid-expiratory flow rate[5] ($FEFR_{50\ to\ 75\ per\ cent}$), the flow rate for the first 1 second of the expirogram ($FEFR_{1.0\ sec.}$), the delayed second flow rate obtained by discarding the first 300 cc's of the expirogram and determining the flow rate over the next 1.0 second ($FEFR_{-300,\ 1.0\ sec.}$), and the delayed 1½ second flow rate, obtained in the same manner as the delayed 1½ second timed vital capacity; except the result is expressed as a flow rate ($FEFR_{-300,\ 1.5\ sec.}$). The manner in which each of these measurements was made is shown in Figure 1. It should be clearly understood that the $FEFR_{1.0\ sec.}$ is precisely the same as the forced expiratory volume (FEV) referred to in British publications[9] and the forced expiratory capacity (FEC) of Miller.[6] This volume is expressed in this study as a forced expiratory flow rate to permit easier comparison with the maximum and mid-expiratory flow rates which are not as logically expressed as a volume. It should also be apparent that the $FEFR_{-300,\ 1\ sec.}$ and $FEFR_{-300,\ 1.5\ sec.}$ can be expressed as a volume without in any way altering the results or relationship to the MBC.

Results

The relationship of the $TVC_{0.15\ sec.,\ 0.75\ sec.\ and\ 1.0\ sec.}$ to the MBC is presented in Figure 2. Although there is a linear relationship between the mean TVC and MBC, the standard deviation in each instance is so

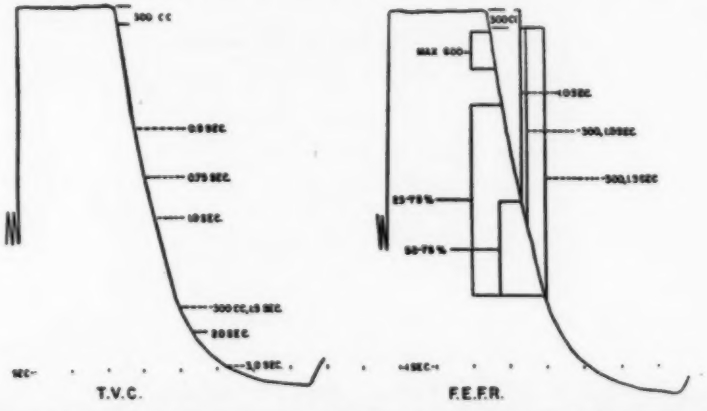

FIGURE 1: Method of Measurement of the Various Forced Expiratory Flow Rates (FEFR) and the Timed Vital Capacities (TVC).

extreme that the usefulness of any of the three TVC's as a substitute for the maximum breathing capacity is seriously limited.

The correlation between the 2.0 sec., 3.0 sec., and −300, 1.5 sec. TVC and the maximum breathing capacity is depicted graphically in Figure 3. The value of the $TVC_{2.0\ sec.}$ as a substitute for the MBC is seriously compromised by the excessive variation of the results and by the fact that there is little increase in the mean $TVC_{2.0\ sec.}$ value after an MBC

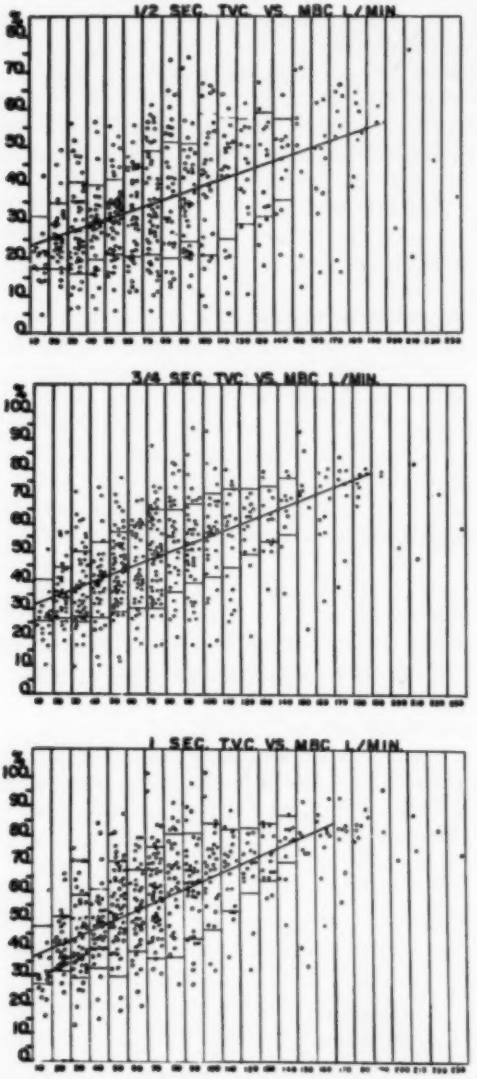

FIGURE 2: The Relationship Between $TVC_{0.5\ SEC.}$, $TVC_{0.75\ SEC.}$, $TVC_{1.0\ SEC.}$ and the MBC. The TVC's are expressed as a per cent of the total VC; the MBC in L/minute. The solid line is drawn as the best fit to the means; the lighter horizontal lines indicate one standard deviation above and below the mean.

of 75 L/minute has been reached. Although the MBC increases from 70 to 140 L/minute, the mean $TVC_{2.0\ sec.}$ increases from 82 to 88 per cent. The $TVC_{3.0\ sec.}$ displays less variation about the mean values than does the 2.0 second; however the 3 second values reach a plateau at an MBC of only 55 L/minute and do not increase by a statistically significant extent thereafter even as the MBC rises to 140 L/minute. The explanation for this appears simple, the mean 3 second TVC for individuals with an MBC of 55 L/minute is 85 per cent of the total TVC; this means that only 15 per cent more of the total vital capacity can possibly be expelled;

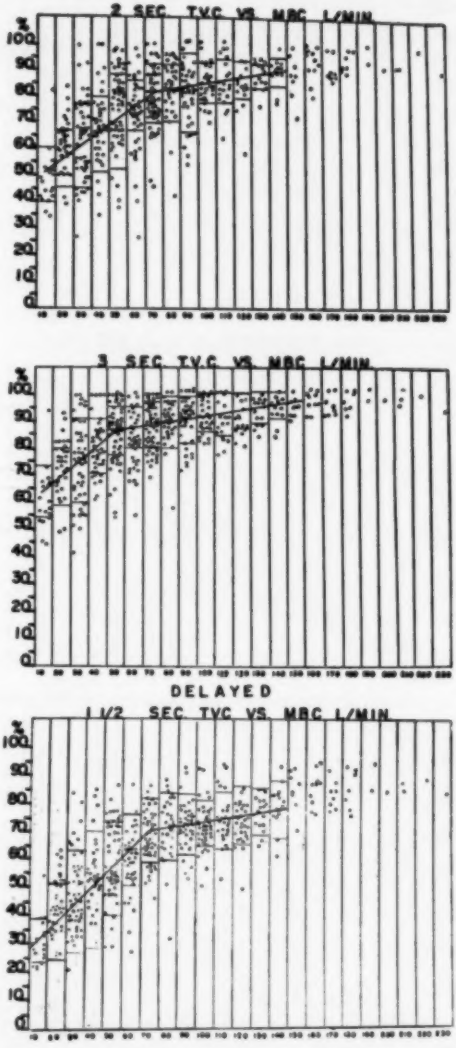

FIGURE 3: The Relationship Between $TVC_{2.0\ SEC.}$, $TVC_{3.0\ SEC.}$, $TVC_{-200,\ 1.0\ SEC.}$ and the MBC in L/minute.

thus with further increase in MBC the 100 per cent value will be approached asymptotically by the mean 3 second value. Regardless of the explanation, the value of the $TVC_{3.0\ sec.}$ as a substitute for the MBC is limited.

The delayed 1.5 second timed vital capacity ($TVC_{-300,\ 1.5\ sec.}$) arose as a result of the observation that the first 0.5 second of the TVC displayed such marked variation from one individual to the other. It was hoped that by eliminating the first 300 cc's of the TVC and making the measure-

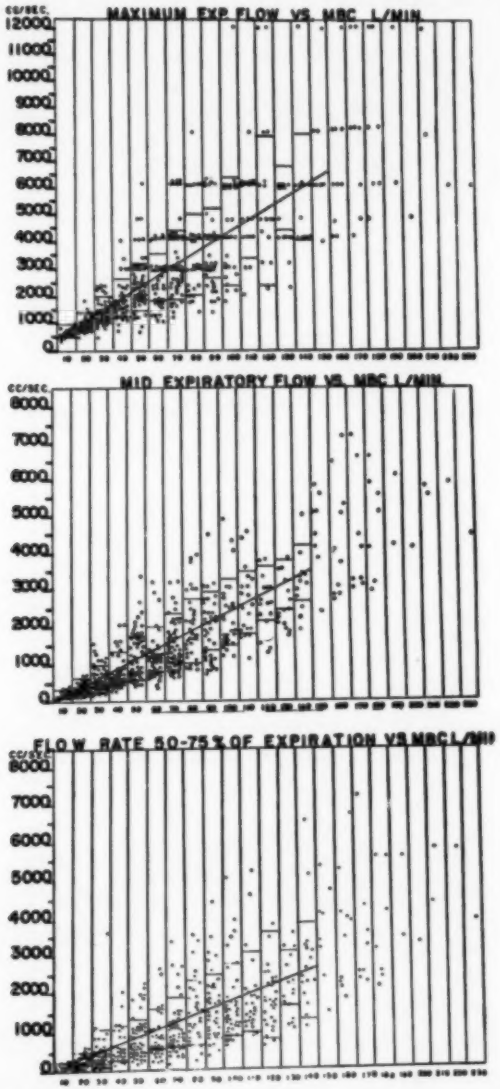

FIGURE 4: The Relationship Between $FEFR_{MAX.-00}$, $FEFR_{25\ TO\ 75\ PER\ CENT}$, $FEFR_{20\ TO\ 75\ PER\ CENT}$, and the MBC. TheFEFR's are expressed as cc/second; the MBC as L/minute.

ment over a period less than 2 seconds, a better correlation would be obtained. From reviewing Figures 2 and 3, it is apparent that the variation is less about the means of the $TVC_{-300,\ 1.5\ sec.}$ than for the 0.5, 0.75, or 1.0 sec.; but not appreciably better than for the 2.0 or 3.0 second TVC. Another similarity to the $TVC_{2.0\ sec.}$ is the fact that the delayed 1.5 sec. TVC reaches a relative plateau with an MBC of 75 L/minute. The only excuse for mentioning and retaining the $TVC_{-300,\ 1.5\ sec.}$ is for comparison with the $FEFR_{-300,\ 1.5\ sec.}$ (forced expiratory flow rate) discussed below.

The comparison between $FEFR_{max.\ 600}$,[3] $FEFR_{25\ to\ 75\ per\ cent}$,[4] $FEFR_{50\ to\ 75\ per\ cent}$,[5] and the MBC are shown in Figure 4. In each instance there is a

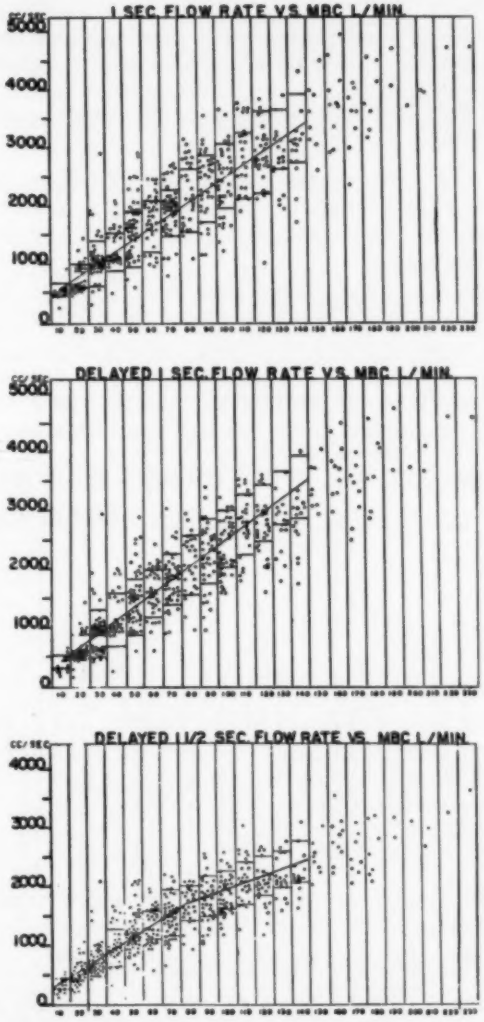

FIGURE 5: The Relationship Between $FEFR_{1.0\ SEC.}$, $FEFR_{-300,\ 1.0\ SEC.}$, $FEFR_{-300,\ 1.5\ SEC.}$ and the MBC.

linear relationship between the means of the $FEFR_t$ and the MBC expressed in liters per minute.

The clustering of the values of the $FEFR_{max.\ 600}$ about 12,000 cc's per second, 8,000 cc's per second and 6,000 cc's per second is an artifact due to the method of measurement wherein the flow rate is measured to the nearest ruled line on the kymograph paper. With a kymograph speed of 1200 millimeters per minute the space between lines represents 1/20 second. At each of these three forced expiratory flow rates the standard deviation is within acceptable limits at an MBC below 40 L/minute, but increases gradually to the point of unacceptability at higher values of MBC. The $FEFR_{25\ to\ 75\ per\ cent}$ (mid-expiratory flow rate) gives the best correlation and the least standard deviation of these three FEFR's. The relationship between the mid-expiratory flow rate and the MBC can be expressed as:

$$\frac{\text{mid-expiratory flow rate in cc/sec.}}{100} \times 4 + 100 = \text{MBC in L/minute.}$$

Figure 5 illustrates the correlation between $FEFR_{1.0\ sec.}$; $_{-300,\ 1.0\ sec.}$ and $_{-300,\ 1.5\ sec.}$ and the MBC. These three flow rates give the best relationship to the MBC and the least standard deviation of any segment of the forced expirogram studied.

The 1.0 sec. and the −300, 1.0 sec. flow rates have a linear relationship to the MBC, at least up to an MBC of 140 L/minute. The −300, 1.5 sec. flow rate can also be expressed as a linear relationship, but changes slope at the 85 L/minute MBC level. The comparatively small and acceptable deviation from the mean of the $FEFR_{-300,1.5\ sec.}$ is the primary reason to recommend it as a substitute for the MBC in comparison to other por-

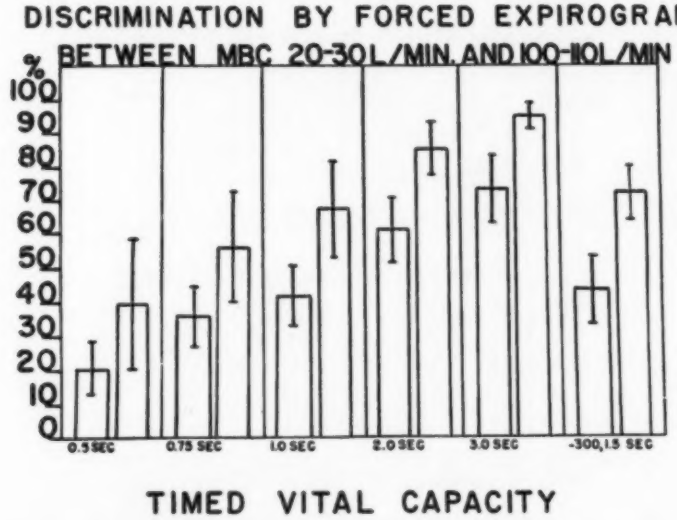

FIGURE 6: The first bar in each column indicates the mean value of that TVC with an MBC of 20-30 L/min.; the second bar indicates the mean value of that TVC with an MBC of 100-110 L/min. One standard deviation above and below the mean is also indicated.

tions of the forced expirogram. The −300, 1.0 sec. flow rate displays less deviation about the mean, in general, than does the 1 second flow rate; however, this difference does not appear to be of sufficient magnitude so as to recommend the additional trouble of calculating the delayed flow rate in comparison to the ease of calculating the $FEFR_{1.0\ sec.}$.

The relationship between these three flow rates and the MBC can be expressed by the following formulae:

$$\frac{\text{1 second flow rate in cc/sec.}}{100} \times 4.6 - 10 = \text{MBC in L/minute}$$

$$\frac{\text{delayed 1 second flow rate in cc/sec.} - 100}{100} \times 4.25 = \text{MBC in L/minute.}$$

These two formulae will be exactly the same if one wishes to express this flow rate as a volume or capacity since it is measured over a period of one second. Since the delayed 1.5 second flow rate changes slope at an MBC of 85 L/minute, the following two formulae are required:

$$\frac{\text{delayed 1.5 second flow rate of 250-1700 cc/sec.} - 50}{100} \times 5 = \text{MBC in L/minute}$$

$$\frac{\text{delayed 1.5 second flow rate above 1700cc/sec.} - 775}{100} \times 9 = \text{MBC in L/minute.}$$

To summarize this section, the relationship between the $FEFR_{-300,\ 1.5\ sec.}$ and the MBC displays the least standard deviation of all segments

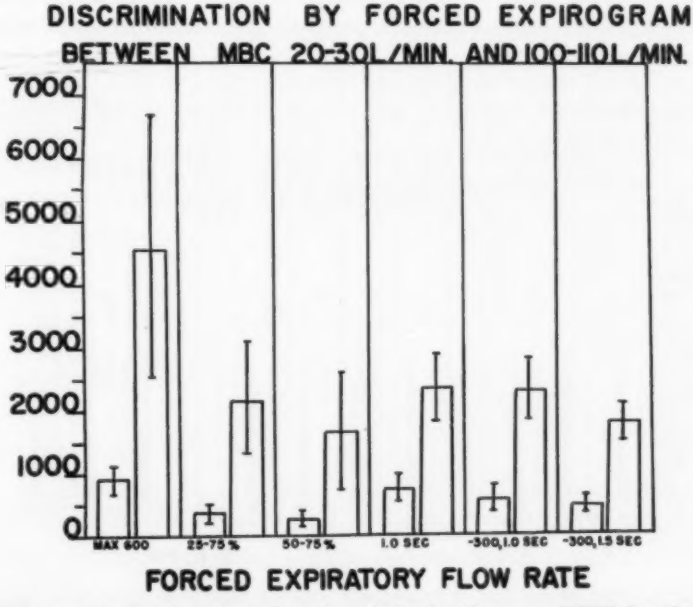

FIGURE 7: The first bar in each column indicates the mean FEFR for that particular segment with an MBC of 20-30 L/min.; the second bar indicates the mean value of that FEFR with an MBC of 100-110 L/min. One standard deviation above and below the mean is indicated.

of the forced expirogram studied. Forced flow rates are much better correlated with the maximum breathing capacity than are timed vital capacities.

In order to determine which portion of the forced expirogram gives the best discrimination, the mean and standard deviation for each of the 12 portions studied were plotted for an MBC level of 20-30 L/minute and 100-110 L/minute. Figure 6 illustrates the results when considering the timed vital capacity.

The $TVC_{-300,\ 1.5\ sec.}$ displays the best ability to discriminate between the low and high MBC levels and with the least standard deviation. The $TVC_{0.5\ sec.}$ provides the poorest discrimination with the greatest standard deviation; the other timed vital capacities studied are more nearly like the 0.5 sec. value than the −300, 1.5 sec.

Figure 7 indicates the ability of the various FEFR's to discriminate between low and high MBC's. The $FEFR_{max.\ 600}$ has a 4.5 times increase with an increase of fivefold in the MBC; but the standard deviation of ±2000cc at the higher level is unacceptable. The $FEFR_{25\ to\ 75\ per\ cent}$ and $FEFR_{50\ to\ 75\ per\ cent}$ display a 5.4 fold mean increase with a fivefold increase in MBC; however, the standard deviation of more than ± 900 cc's per second seriously comprimises the value of these two flow rates. The $FEFR_{-300,\ 1.0\ sec.}$ appears somewhat superior to the $FEFR_{1.0\ sec.}$ in respect to discriminating a fivefold increase in MBC's; the former has a 3.7 fold increase with a standard deviation of ± 476 cc's per second; whereas, the $FEFR_{1.0\ sec.}$ has only a threefold increase and a standard deviation of ± 567 cc's per second. The $FEFR_{-300,\ 1.5\ sec.}$ has a standard deviation of ± 317 cc's per sec. and a 3.5 fold increase with a fivefold increase in MBC.

In summary, the $FEFR_{-300,\ 1.5\ sec.}$ appears to be the best of the various portions of the forced expirogram to discriminate between MBC's with a fivefold difference, especially since a low standard deviation about the

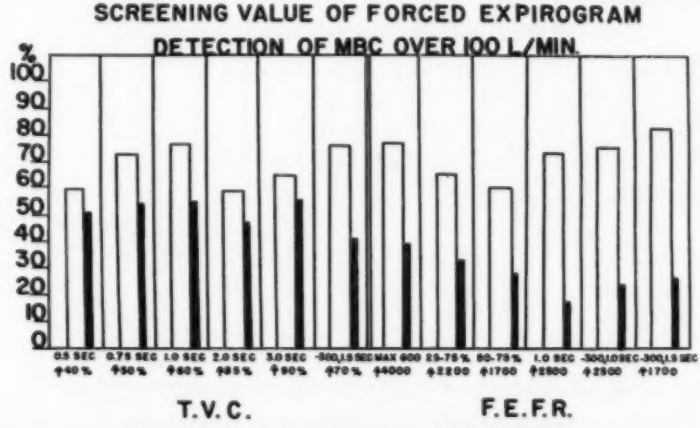

FIGURE 8: The percentage of individuals with an MBC over 100 L/min. correctly "caught" in the screen is indicated by the open bar; the percentage of false positives "caught" by the screen is indicated by the solid bar. The arrow and percentage figure indicates the level at which the screen was set for the TVC's; the arrow and numbers indicate the flow rate in cc/sec. at which the screen was set for the various FEFR's.

mean seems to be more important in order to obtain a greater difference in means.

The data depicted in Figures 2 to 5 were next analyzed to determine which portion of the forced expirogram could best be employed as a screening tool. The most desirable segment for screening purposes would divide the patients into three groups; those whose MBC was above 100 L/minute and could be assumed to have reasonably good ventilatory function; those who were ventilatory cripples insofar as physical exertion was concerned' and whose MBC was less than 50 L/minute; and an intermediate group who should have further study to ascertain their physiological state from a ventilatory point of view. The best screening test would be the one to detect the highest percentage within a given MBC range with the lowest number of false positives.

Figure 8 indicates graphically the screening value of each portion of the expirogram insofar as percentage of individuals whose MBC was over 100 L/minute was concerned. The percentage of false positives for each group is also shown.

The best screening test will be that one with the greatest difference between the percentage correct and the percentage of false positives. The $TVC_{-300,\ 1\text{-}5\ sec.}$ is the best of the timed vital capacities; however, 41 per cent false positives in a screening test is not acceptable. The $FEFR_{1\text{-}0\ sec.}$ and the $FEFR_{-300,\ 1\text{-}5\ sec.}$ are of equal value in that the difference between the number correctly screened and the number of falce positives is the same in both instances. However, 18 to 26 per cent false positives are still a good many to accept in this sort of screening test. The percentage of false positives can be reduced by lowering the flow rate level at which the screen is set; however, this will result in a sacrifice of the number of individuals correctly selected.

Figure 9 illustrates the screening value of the segments of the forced expirogram relative to an MBC less than 50 L/minute. In this instance also the $TVC_{-300,\ 1\text{-}5\ sec.}$ is by far the best of the various timed vital capac-

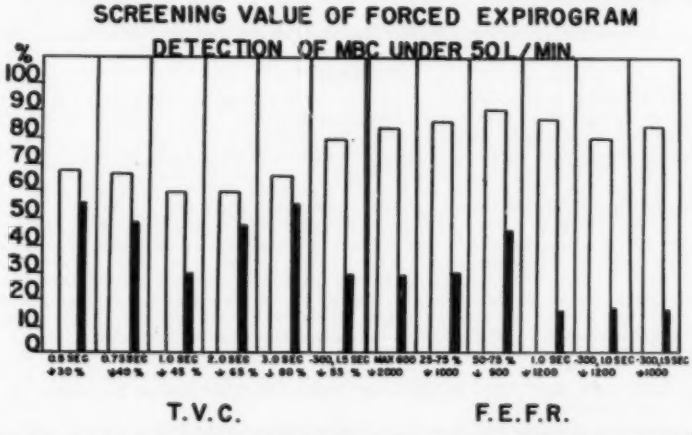

FIGURE 9: The percentage of individuals with an MBC under 50 L/min. correctly "caught" in the screen is indicated by the open bar; the percentage of false positives "caught" by the screen is indicated by the solid bar. As in Figure 8, the arrows indicate the level at which the screen was set for each of the TVC's and the FEFR's.

ities studied. The $FEFR_{1.0\ sec.}$ and the $FEFR_{-300,\ 1.5\ sec.}$ are again the same and appreciably better than any other FEFR. There are 16 per cent false positives caught in this screen. Although these results seem to favor slightly the $FEFR_{-300,\ 1.0\ sec.}$, this should not be construed as suggesting the abandonment of the $FEFR_{1.0\ sec.}$ ($FEV_{1.0\ sec.}$, $FEC_{1.0\ sec.}$) by those laboratories where this is used.

Discussion

When either performing or ordering a timed vital capacity (TVC), an expiratory flow rate (FEFR), forced expiratory volume (FEV) or forced expiratory capacity (FEC) for a patient, the physician should have clearly in mind why he is doing this and what he expects to learn from it. If he plans to use the expirogram as either a substitute for, or check on the validity of, the MBC, it is apparent from this study that the widely used timed vital capacity is a rather poor choice and should be abandoned for this purpose. It is further evident that if the physician has the above purpose in mind any segment of the FEFR studied is of greater value than any portion of the TVC.

The relationship between the various portions of the FEFR's and MBC's of less than 50 L/minute is of some interest. The small variation about the mean of the segments of FEFR's in the low MBC range as compared to the variations noted with higher MBC's is rather striking. This phenomenon suggests that the flow rates with the lower MBC's is determined by something which does not influence to the same extent the flow rate with higher values of MBC. Although further work will be required to gain data to support such an explanation, the most likely explanation is that with MBC's below 50 L/minute the forced expiratory flow rate is primarily a function of the characteristics of the airway and is not appreciably influenced by muscle strength, neuromuscular coordination or other factors which have a greater proportionate influence on the flow rate at higher levels of MBC.

The greatest application of the concept of FEFR (or FEV or FEC) would appear to be as a screening procedure. Spirometers currently available can be easily modified to give direct readings of $FEFR_{1.0\ SEC.}$; $_{-300,\ 1.0,\ SEC.}$ OR $_{-300,\ 1.5\ SEC.}$* It is the opinion of the author that the kymograph used for recording FEFR should have a paper speed of at least 8,000 millimeters per minute. Within limits, the faster the speed the less the error due to the mechanics of measuring the forced expirogram. If one wished, every patient seen in a busy physician's office or admitted to a general hospital could be quickly screened by means of such apparatus. Such a screening test would also have application to various industrial health problems and could be done much more quickly than routine radiographs and from the point of view of disability would also be much more logical.[8]

When one recalls the several variables mentioned in the introduction which can influence the MBC, it is surprising that one obtains as good a correlation between MBC and FEFR as was obtained. If each of these several variables were determined in a group of patients with varying levels of MBC,at least some of the controversy could be resolved regarding just what is being measured by the performance of an MBC, and which of the several determinants have the greatest influence on MBC.

SUMMARY

Various portions of the forced expirograms have been determined from recordings obtained by means of a rapid kymograph and compared with regard to how well each could serve as a substitute for the MBC; the ability of each to discriminate between a fivefold difference in MBC, and the applicability of each as a screening tool. There are two broad types of segments to be studied on the forced expirogram, the timed vital capacity (TVC) and the forced expiratory flow rate (FEFR). The 0.5, 0.75, 1.0, 2.0, and 3.0 second TVC's gave poor results for the three broad functions being evaluated. A delayed 1.5 sec. TVC ($TVC_{-300,\ 1.5\ SEC.}$) gave the best results of all the TVC's evaluated. By far the best results were obtained by considering the FEFR. The max. 600, 25 to 75 per cent, 50 to 75 per cent, 1.0 sec., —300, 1.0 sec. and —300, 1.5 sec. segments were evaluated. The —300, 1.5 sec. gave slightly better over-all results with the least standard deviation for correlation with the MBC, discriminatory ability and screening value; however, it was not enough better than the 1.0 sec. value to suggest that the latter be abandoned by those laboratories using this test in the form of either a 1.0 sec. forced expiratory volume or expiratory capacity. The results of this study do suggest that the laboratories using either the maximum, mid-expiratory or three-fourths expiratory flow rates might re-examine the information furnished by these segments and perhaps change.

The suggestion is advanced that the determination of the FEFR has its chief application as a screening tool for use in the physician's office, the general hospital and

*The Godart Pulmometer has been adapted to this purpose for our laboratory by Instrumentation Associates, New York, New York.

various industrial situations. A secondray ues would be as a check on the validity of the MBC, especially if one had reason to question the cooperativeness of the patient under study.

ACKNOWLEDGEMENT: The invaluable technical assistance of Kenneth Dorton, Joan Brown and Pauline Faulkner is gratefully acknowledged.

RESUMEN

Se determinaron varias partes de gráficas de experación forzada tomadas de registros obtenidos por medio de un kimograma rápido y se compararon para saber hasta qué grado pueden servir para como substituto de la CMR (Capacidad Máxima Respiratoria); también para saber la cápacidad de distinguir en una diferencia quíntuple en CMR y la aplicabilidad de cada parte como elemento de detección.

Hay dos grandes porciones de los segmentos de la gráfica que han de estudiarse en el expirograma forzado, la Capacidad Vital por Segundos (CVS) y la estimación del flujo expiratorio forzado (FEFR en Inglés que puede codificarse en Español como: Flujo Expiratorio Forzado: FFF). (N. del T.)

La CVS (Capacidad Vital por Segundos) de 0.5, 0.75, 1.0, 2.0 y 3.0 dió resultados deficientes para la valuación de las tres grandes funciones estimadas. Much mejores fueron los resultados considerando el FFF. Los segmentos: máximo 600, 25-70 por ciento, 1.0 segundo, —300, 1 seg. y —300, 1.5 seg. dió en general, mejores resultados con la menor desviación estandard para la correlación con la CMR, la capacidad discriminatoria y valor de detección; sin embargo no fué suficientemente mejor que el valor de 1.0 segundo para sugerir que el último deba abandonarse por los laboratorios que usan esta prueba en la forma ya sea de volumen expiratorio forzado del segundo o capacidad expiratoria. Los resultados de este estudio, sugieren que los laboratorios que usen ya sea el flujo máximo, medio-expiratorio o tres cuartos expiratorio, podrían reexaminar la información que obtienen por estos segmentos y quizás cambiar.

Se adelanta la sugestión de que la determinación del FFF (FEFR) tiene su aplicación principal como elemento de detección para uso en el consultorio, el hospital general y varias condiciones industriales. Un uso secundario podría esr para corroborar la validez de la CMR, especialmente si se tienen dudas sobre la cooperación del enfermo que se estudia.

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Aimed Bronchography

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With the cooperation of the bronchologist and roentgenologist, new and more complete methods have been evolved in pulmonary diagnosis and therapy. Such special procedures are, among others, (1) bronchography itself, (2) exact localization of pulmonary changes by segmentology, (3) the so-called "blind" biopsy, based on the previous system, (4) bilateral fluoroscopic removal of bronchoscopically invisible, but opaque, foreign bodies and (5) fluoroscopic bronchial aspiration in premature infants. These and similar procedures effectively support the work of an up to date chest physician. A newer and more complete method is "aimed bronchography."

During bronchography, we frequently observe that the bronchi of one or other pulmonary unit (lobe or segment) are not, or only partially, filled (dead-tree effect). This phenomenon usually appears in that portion of the lung where roentgen changes were observed during previous x-ray examination. However the "dead tree effect" may also appear in cases with previous negative x-ray findings.

This may mean that a pathological or a functional process is hidden in the unfilled portion of the lung, or it may depend on errors of bronchography. Filling defect or interrupted filling can be caused by too small an amount of the contrast fluid and also by pathological changes of the bronchi. Sometimes when inadequate amounts of contrast fluid are used, the fluid does not penetrate as far as the peripheral bronchi to be examined. Furthermore, if the amount of filling is inadequate one may be unable to observe physiological or pathological movements of the bronchi which are an essential part of the bronchography. The bronchogram may be deficient if the examination is done in a faulty position or if the film is exposed too soon. Incomplete bronchial filling, deficient and easily misanalyzed bronchograms may be caused by extrabronchial factors. Phrenic paralysis, conditions after chest injuries and operations, pulmonary diseases with destruction of elastic elements, pneumothorax, emphysema, etc. may diminish the respiratory sucking effect, which is an essential factor in transporting the contrast fluid. Adequate filling of the bronchi is frequently prevented by voluminous thick pus or blood; therefore, in the presence of such secretion or blood, preliminary bronchoscopic aspiration is indicated. If the mucosa in the orifice of a lobar or segmental bronchus is congested or cicatrized, or if the lumina of the bronchi are obstructed with thick secretion, it can be concluded that with routine bronchography the bronchi distal to the stenosis will not be filled.

In every case where bronchography is indicated and performed, but fails to yield adequate information because of the "dead tree effect," the filling should be completed with "aimed bronchography." Naturally, "aimed bronchography" only supplements routing bronchography and never supplants it. Aimed bronchography serves to reveal the cause of filling defects and the pathologic lesion in the distal parenchyma.

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For this reason, Metras,[1] Homma[2] and others insert a special and properly curved catheter into the bronchus of the involved lobe or segment under fluoroscopic guidance without bronchoscopy. In our experience with cases of substantially stenosed bronchi (narrowed by congestion or scars, obstructed by tumor, torsion or angulation), we did not succeed with this method. In the majority of cases, the soft and relatively thick Metras-catheter cannot be inserted "blindly" into the grossly stenosed or obstructed bronchial orifice. Maasen with his catheter, which has inflatable cuffs, occludes the bronchial system above and below the orifice of the bronchus aimed at and injects the contrast material "passively" into the lung portion in question.

We introduce our special tubes into the narrowed bronchi under bronchoscopic and fluoroscopic guidance. Tubes were made for different

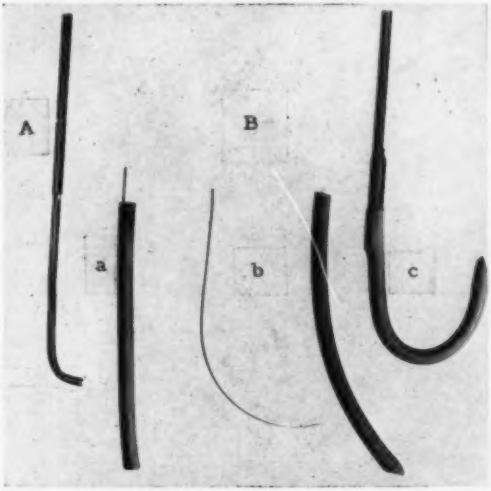

FIGURE 1: Photos of instruments for "aimed bronchography." Tube A was made for aimed bronchography through a short but substantial stenosis of a major branch originating from the main, stem or lower lobe bronchus. The thin end-portion, made from brass, is pliable so that it can be bent for any bronchus to be examined, and is made in such a way that it can pass the lumen of a 7, 8 or 9 mm. bronchoscope. This type of tube was used for both upper lobe bronchi and the superior segmental bronchi of the lower lobes (see arrow in Fig. 6, D).

Tube B has three types of changeable ends. Each of them consists of fine metal spring and a double rubber tubing. Four types of spring are shown in Fig. 1, B; straight (a), simple curved (b) and double curved (c) tubings. The flat spring is inserted into one of the two canals of the rubber tubing. This canal ends blindly, the other is open for aspiration of secretions or for instillation of contrast or other fluids. The spring keeps the rubber tubing firm for insertion and it is flexible only in one plane. By this mechanism, the tube is more directible than any other flexible kind. e.g. the tube with spiral, flexible end which are unsuitable for this purpose because of its leakiness Other kinds of tubes such as those ending in plastic tubing are also useless because, after being straightened, it takes time for the tubing to return to its original curve. Our tubes, after being straightened in the bronchoscope during insertion, return to their normal curve immediately after passing the distal end of the bronchoscope.

The spring and rubber tubing are firmly fixed to the distal end of the tube so that it will not slip.

The straight tubing (a) was used for the right middle lobe bronchus and the basal bronchi of the lower lobes; the simple curved tubing (b) for the right middle lobe or lingular bronchus and the superior segmental bronchi of the lower lobes, but it may also be used for the posterior or anterior segmental bronchus of the right upper lobe. The double curved tubes may be useful in bronchial branchings of both upper lobes directed toward the apex.

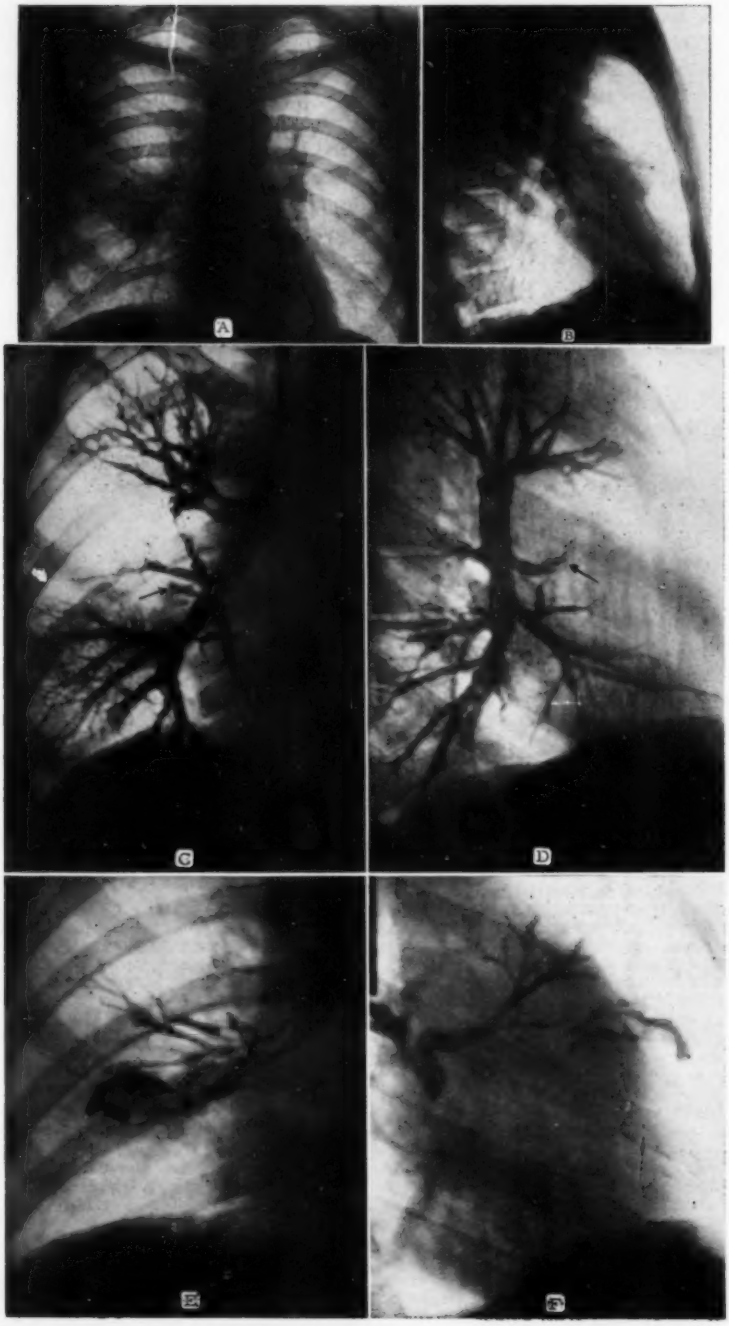

FIGURE 2, Case 1: AP and lateral roentgenograms (A and B) showing spotted density in the right middle lobe region.

AP and lateral bronchograms of the right lung (C and D) show a normal branchial tree except for an incomplete filling in the right middle lobe (see arrows).

AP and lateral "aimed bronchograms" (E and F) revealed an unevenly bordered abscess cavity in the lateral segment of the right middle lobe.

types of cases (Fig. 1). Some tubes are quite rigid, but pliable, others are flexible but hard enough for insertion into the narrowed lumina through the bronchoscope.

With this method, 41 examinations were performed in the two-year period (April, 1952 - April, 1954). These cases grouped according to the site of filling were as follows:

Right upper lobe	3
Left upper lobe	4
Right middle lobe	19
Lingula	2
Right superior segment	8
Left superior segment	3
Left pos. basal segment	2
Total	41

Cases according to diseases:

Bronchiectasis, Bronchitis deformans	15
Pulmonary tuberculosis (stenosis, cavum, bronchiectasis)	6
Pulmonary abscess	5
Tumor	2
Normal filling	13
Total	41

We utilized this method in every case of filling defect (dead-tree effect) involving a pulmonary unit (lobe or segment) with positive or negative x-ray finidings. We often obtained surprising results as is evident from the following examples:

Case 1: A.H., 25 year-old man, became feverish after tonsillectomy, and expectorated brownish-yellow pus. After antibiotic treatment, fever and sputum decreased, but subfebrility and moderate expectoration continued for about two months. Roentgenogram showed a spotted density in the right middle lobe region (Fig. 2, A and B). Discharge of brownish-yellow pus from the right middle lobe bronchus was observed bronchoscopically. After careful aspiration of these secretions, bronchograms showed a normal bronchial tree except for a filling defect in the right middle lobe bronchi (Fig. 2, C and D).

Aimed bronchography revealed an unevenly bordered abscess cavity in the lateral segment of the right middle lobe (Fig. 2, E and F). After unseccussful attempts at bronchoscopic treatment, lobectomy was performed.

Comment: After tonsillectomy, an abscess cavity appeared in the lateral segment of the right middle lobe, but its presence could be demonstrated only by aimed bronchography.

Case 2: I.K., 23 year-old man, had hemoptysis on occasions since 1948. Roentgenograms showed some indistinct densities in the left lower lobe regions (Fig. 3, A and B). In 1953, the increased bleeding caused anemia, and he received repeated blood transfusions. Left bronchography was done, and the superior segment of the left lower lobe did not fill (Fig .3, C and D). June, 1953: Discharge of fresh blood from the above mentioned bronchus was observed by bronchoscopy. With aimed bronchography, a small walnut sized abscess cavity filled up the lower portion of the left superior segment (Fig. 3, E and F). He coughed up the thick contrast fluid (Joduron B) and discharged a small (3 mm. in diameter) metal foreign body (Fig. 3, G). Since then hemoptysis never recurred. Three months later, control aimed bronchography was done which demonstrated that the abscess cavity had completely healed.

Comment: A foreign body in the superior segment of the left lower lobe caused an abscess with severe hemoptysis for five years. The abscess was demonstrated by aimed bronchography. In this case, aimed bronchography was not only a correctly applied diagnostic procedure, but also happened to be a therapeutic maneuver.

Case 3: F.G., 46 year-old man. For three years, he had frequent colds, complicated many times by pneumonia. With the last attack, the amount of mucopurulent secretion increased. The sputum was negative for acid-fast bacilli. On the roentgenograms, the right diaphragm was moderately drawn up by adhesions, and there was slight density in the right middle lobe region. With bronchoscopy, a large amount of mucopurulent secretion was aspirated from the right bronchial system, and the orifice of the right middle lobe bronchus which was filled for only a short distance (Fig. 4, A).

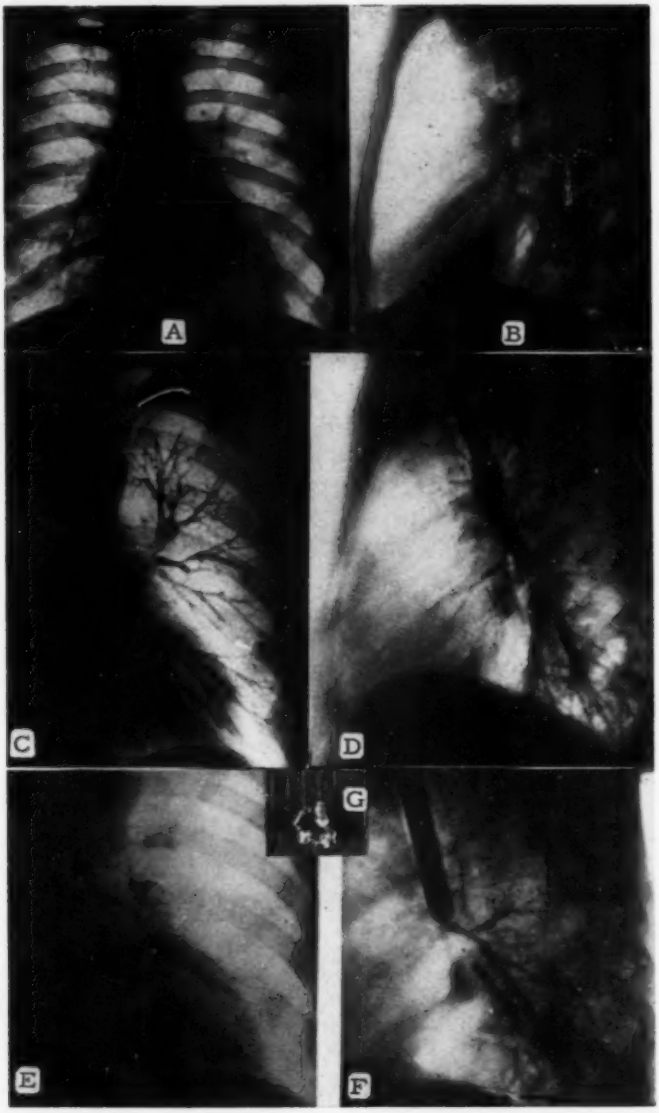

FIGURE 3, Case 2: AP and lateral bronchograms (A and B) show some indistinct densities in the left lower lobe region.

AP and lateral bronchograms of the left lung (C and D) show absence of filling in the superior segment of the left lower lobe; two subsegmental bronchi of this segment appear mutilated (see arrows).

AP and lateral "aimed bronchograms" (E and F) revealed a walnut sized abscess cavity in the lower portion of the superior segment of the left lower lobe.

A small metal foreign body (G), 3 mm. in diameter, which was discharged with the contrast fluid, caused the abscess to persist for five years.

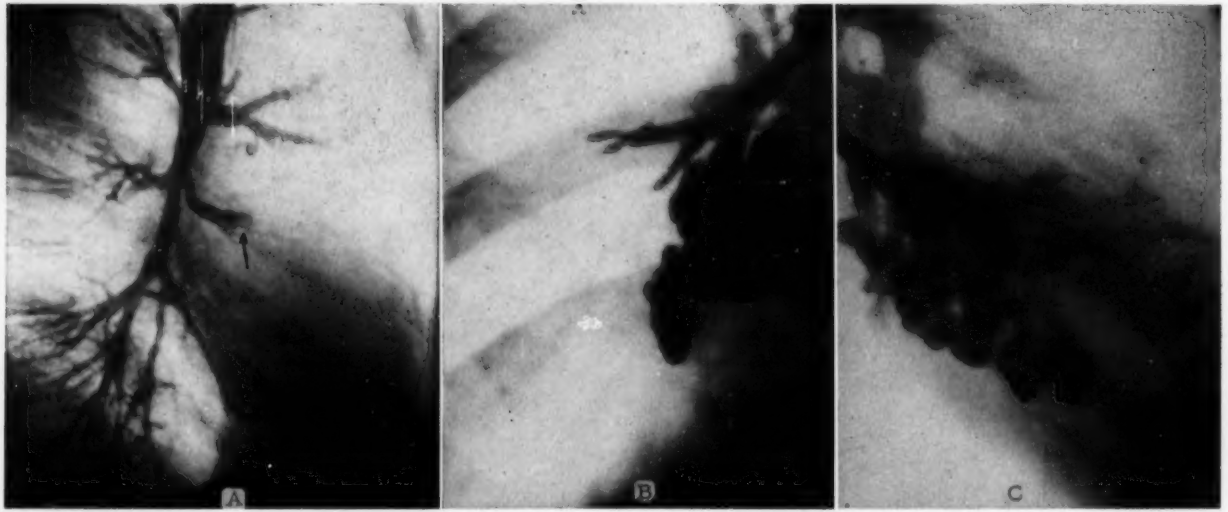

FIGURE 4, Case 3: Lateral bronchogram (A) of the right lung shows the right middle lobe bronchus filled for only a short distance (see arrow). AP and lateral "aimed bronchograms" (B and C) revealed extensive saccular bronchiectasis in the medial segment of the right middle lobe.

Aimed bronchography revealed extensive saccular bronchiectasis in the medial segment of the right middle lobe (Fig. 4, B and C). At the time, surgery was postponed for cardiac reasons.

Comment: Bronchiectasis with unknown etiology in the medial segment of the right middle lobe could be diagnosed only by aimed bronchography.

Case 4: B.P., 39 year-old woman, had pulmonary pathology since 1952. At that time, a tuberculous cavity was visible on the roentgenograms in the superior segment of the right lower lobe. In 1953, antibiotic treatment was administered. The cavity disappeared and the sputum became negative for acid-fast bacilli.

In 1955, the subfebrility and strong cough recurred, but no cavity could be demonstrated either with roentgenography or with planigraphy (Fig. 5, A, B and C). With routine bronchography, the bronchi of the apical segment of the right lower lobe did not fill (Fig. 5, D). With aimed bronchography, a walnut-sized cavity filled in this segment (Fig. 5, E and F). Segmental resection was performed.

Comment: Tuberculous cavity, undetected with routine roentgenography, planigraphy and routine bronchography was demonstrated by aimed bronchography.

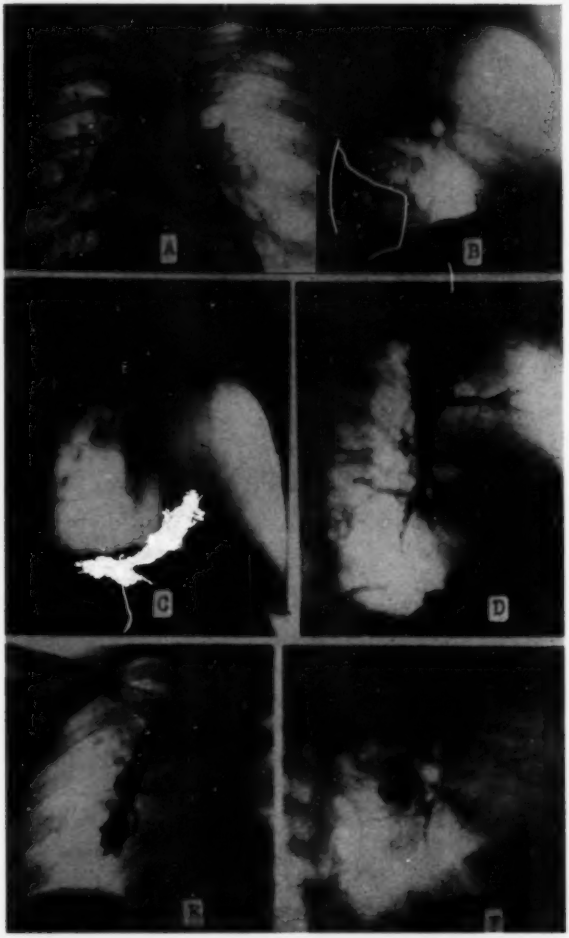

FIGURE 5, Case 4: No cavity could be demonstrated with AP and lateral roentgenograms and lateral planigram (A, B and C). Lateral bronchogram of the right lung (D) shows "dead tree effect" in the superior segment of the right lower lobe.
AP and lateral "aimed bronchograms" (E and F) revealed a tuberculous cavity in this segment.

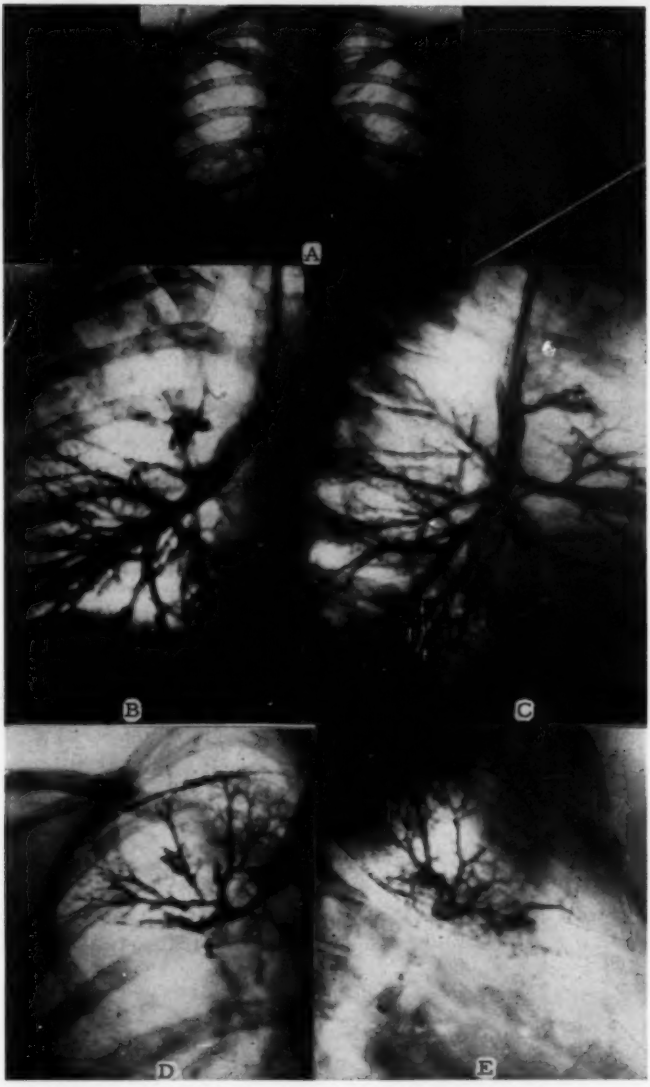

FIGURE 6, Case 5: AP roentgenogram (A) shows no abnormal density in the suspected right upper lobe region. In AP and lateral bronchograms (B and C) filling of the right upper lobe bronchi was prevented by extreme cicatrical stenosis of the right upper lobe bronchus caused by tuberculous bronchitis.

AP and lateral "aimed bronchograms" (D and E), which were performed with a special tube ending in a rigid but pliable tube 1 mm. in diameter (see arrow), show the few mm. of the lobar bronchus extremely narrowed; the anterior segmental bronchi with moderate knotted bronchiectasis and the rest of the bronchi with signs of bronchitis deformans.

Case 5: I.V., 27 year-old woman, tuberculous changes were diagnosed in the right upper lobe in autumn, 1950. During three years of treatment, she received 2300 gm. PAS and 500 tablets of INH. The sputum became negative for tubercle bacilli. In autumn, 1952, the secretion increased in volume, and with bronchoscopy, a cictrical stenosis (1 mm. in diameter) was found in the orifice of the right upper lobe bronchus, and a fairly large amount of mucopurulent secretion was seen. In spring, 1953: active disease recurred with high fever; bronchoscopy repeated with essentially the same findings. From the old stenosis and profuse suppuration, we suspected bronchiectasis in the distal parenchyma, but no abnormal shadow or sign of shrinkage could be observed on roentgenograms (Fig. 6, A).

On routine bronchograms, the right upper lobe bronchi did not fill—only the anterior bronchus for a short distance (Fig. 6, C and D). Because of the extremely narrowed orifice, a special tube was employed which ended in a rigid pliable tube 1 mm. in diameter with a short right angle curve (Fig. 1 and Fig. 6). With this instrument, we successfully filled the bronchi. The first few mm. of the lobar bronchus were extremely narrowed. The bronchi of the anterior segment showed moderate knotted bronchiectasis, and the rest of the bronchi showed signs of bronchitis deformans (Fig. 6 ,D and E).

Comment: From tuberculous bronchitis, irreversible fibrotic stenosis developed. Aimed bronchography revealed that bronchiectasis is developing from bronchitis deformans, but the whole lobe is still aerated. Lobectomy was performed.

SUMMARY

The authors propose a special method of "aimed bronchography" in cases of "dead tree effect." Special tubes inserted into the bronchi aimed through the bronchoscope under fluoroscopic guidance. Surprising and significant results are demonstrated by this method.

RESUMEN

El autor propone un método especial de "broncografía hacia el blanco" en casos de "efecto del ábol muerto."

Se insertan tubos especiales através del broncoscopio y bajo la guía fluoroscópia.

Se obtienen por este método, sorprendentes y significantes resultados.

RESUMÉ

Les auteurs proposent une méthode spéciale de "bronchographie dirigée" dans les cas de "bronches en bois mort."

Des tubes spéciaux sont introduits dans les bronches, dirigés à travers le bronchoscope sous surveillance radioscopique. Des résultats surprenants et nets sont obtenus par cette méthode.

ZUSAMMENFASSUNG

Die Autoren schlagen eine spezielle Methode der "erleichterten Bronchographie" vor in Fällen von "dürrem - Ast - Effekt."

Spezialkanülen werden in die Bronchien eingeführt mit Hilfe des Bronchoskopes und unter Kontrolle des Röntgenschirmes. Mit dieser Methode lassen sich überraschende und wesentliche Ergebnisse erzielen.

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Comparative Results in the Use of Two Commercial PPD Skin Tests in 569 Admissions*

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In recent years there has been much speculation among tuberculosis specialists as to the probability that the incidence of proved pulmonary tuberculosis with negative tuberculin reaction is increasing. This study was undertaken to determine the role of intermediate and second strength PPD in the diagnosis of tuberculosis and in addition, to determine if possible whether there might be any difference in the manufacture of PPD. With this in mind, two brands of PPD, Parke, Davis and Merck, have been used in the routine testing of all newly admitted patients to the hospital. The dosage given initially was 5 T.U. or 0.0001 mg. PPD. One milliliter of one brand PPD was injected into the skin of the volar surface of one forearm just below the elbow and an equal amount of the other brand PPD was injected into the skin of the other arm in the same area. If these tests were negative the same strength intermediate O.T. was given the following week in most cases and if the patient again showed no reaction a second strength PPD was given. However, if this proved to be negative a second strength O.T. was given.

A registered nurse in charge of clinics and experienced in tuberculin testing has given all of the tests and the reading of the tests has been made by the author of this paper. The degree of induration has been measured in millimeters at 48 hours and 72 hours and recorded as such. Where undue redness occurred without induration the tests were repeated. The degree of induration was recorded under four headings; namely, 0 mm. to 5 mm., 6 mm. to 10 mm., 11 mm. to 20 mm., and 21 mm. and over.

This is a report on the findings in 569 patients admitted to the Central Florida Tuberculosis Hospital. Table 1 reveals that 500 of these cases were positive and 69 of them had a negative intermediate PPD test on both arms. Of the 500 patients reacting positively to intermediate PPD 461 had proved tuberculosis, 28 were infected with atypical acid-fast bacilli and 11 had no clinical tuberculosis.

Of the 69 patients reacting negatively to intermediate PPD 24 had proved tuberculosis. Seven of these were taking steroids, 10 were positive to intermediate O.T. and 7 were positive only to second strength PPD.

With the exception of the patients receiving steroids none was terminal or in critical condition. It has long been known that there is a loss of allergic response in patients receiving steroids. Of the remaining 45 cases reacting negatively to intermediate PPD seven were infected with atypical acid-fast bacilli, seven showed x-ray evidence of pulmonary tubrculosis, but had negative cultures, and 31 had no evidence of clinical tuberculosis.

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*Presented at the Annual Meeting, Southern Chapter, American College of Chest Physicians, Atlanta, Georgia, November 15-16, 1959.

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Fifteen of the patients originally tested were positive to one brand tuberculin, but were negative to the other. On re-testing all were found to be positive to both tuberculins. The fact that two intermediate skin tests were done simultaneously in all our cases was in effect a re-test in all cases.

Table 2 gives a comparison between the degree of induration caused by the two brands of intermediate PPD at 48 hours and 72 hours. The degree of induration was recorded under four headings; namely, 0-5 mm., 6 mm. to 10 mm., 11 mm. to 20 mm., and 21 mm. and over. It will be seen that in 81 per cent of the cases at 48 hours and in 80.6 per cent of the cases at 72 hours the indurations caused by the two tuberculins agreed within bracket. Where the indurations changed in diameter from one bracket to another at 48 hours Merck was in a lower bracket than was Parke, Davis in 5.3 per cent of the cases, and at 72 hours was in a lower bracket in 6.8 per cent of the cases. Merck was in a higher bracket than Parke, Davis at the end of 48 hours in 13.6 per cent of the cases and at 72 hours in 12.6 per cent of the cases.

Table 3 gives a comparison of the changes in the degree of induration caused by Merck PPD between 48 hours and 72 hours and between the changes in the degree of induration caused by Parke, Davis PPD between 48 hours and 72 hours. In 79 per cent of the Merck cases and in 75 per cent of the Parke, Davis cases there was no change within bracket between 48 hours and 72 hours. In 18:6 per cent of the Merck cases and in 20.8 per cent of the Parke, Davis cases there was a smaller induration within bracket at 72 hours than at 48 hours. In only 2.4 per cent of the Merck cases and 4.2 per cent of the Parke,Davis cases was there a larger degree of induration at 72 hours than at 48 hours.

Table 4 gives the actual change in degree in induration in millimeters. It will be observed that there was little difference in the change in

TABLE 1—RESULTS OF 569 HOSPITAL PATIENTS TESTED WITH PPD AND O.T.

	No.	per cent
PPD Intermediate Positive		
Number of Cases	500	100
TB Proved	461	92.2
Atypical	28	5.6
No Clinical TB	11	2.2
Number of Cases Negative to Intermediate PPD	69	12.1
PPD Intermediate Negative OT Intermediate Positive		
TB Proved	10	1.2
PPD Intermediate Negative OT Intermediate Negative PPD 2nd Strength Positive		
TB Proved	7	1.2
TB Proved Steroids	7	1.2
TB Proved TOTAL	24	4.2
X-Ray Evidence of TB Negative Culture	7	1.2
Atypical Aci-Fast Bacilli	7	1.2
No Clinical TB	31	5.4
TOTAL	45	8.0

degree of induration caused by the two commercial tuberculins 48 hours to 72 hours, whereas when Merck Intermediate PPD and Parke, Davis Intermediate PPD are compared at the end of 48 hours Merck Intermediate PPD is found to have produced a greater degree of induration than Parke, Davis Intermediate PPD in 31.5 per cent of the cases with an average of 3.6 mm. Parke, Davis Intermediate PPD, on the other hand, showed greater degree of induration than Merck Intermediate PPD at the end of 48 hours in 15.5 per cent of the cases with an average of 3.7 mm.

Table 5 gives the size of induration to intermediate PPD or O.T. in relation to age and race. Only 500 positive reactors are included in the table. In the last column of this table the percentages of the different age groups are recorded. The majority of cases will be found in the upper age brackets.

Fourteen (2.8 per cent) of the patients with proved pulmonary tuberculosis had indurations between 1 and 5 mm. Again 65 (13 per cent) of the patients had reactions which were less than 11 mm. in diameter. The indurations were above 11 mm. in all age groups in 84.2 per cent of the cases. Surprisingly the age group above 70 years had indurations of

TABLE 2—COMPARISON BETWEEN DEGREE OF INDURATION 48 HOURS AND 72 HOURS—PARKE, DAVIS & MERCK

48 Hours	White		Negro		Total	
	No.	per cent	No.	per cent	No.	per cent
PD & Merck agree within Bracket	305	78.5	157	86.5	462	81.1
21 mm. or over PD	12		3		15	
11-20 mm. Merck		3.1		1.7		2.6
11-20 mm. PD	12		2		14	
6-10 mm. Merck		3.1		1.2		2.5
6-10 mm. PD	1				1	
0-5 mm. Merck		0.2				0.2
0-5 mm. PD	8		1		9	
6-10 mm. Merck		2.1		0.6		1.6
6-10 PD	31		13		44	
11-20 mm. Merck		8.0		7.3		7.7
11-20 mm. PD	19		5		24	
21 mm. and over		5.0		2.7		4.3
TOTAL	388	100	181	100	569	100
72 Hours						
PD & Merck agree within Bracket	307	79.1	151	83.4	459	80.6
21 mm. or over PD	7				7	
11-20 mm. Merck		1.7				1.2
11-20 mm. PD	23		6		29	
6-10 mm. Merck		6.0		3.3		5.1
6-10 mm. PD	2		1		3	
0-5 mm. Merck		0.5		0.5		0.5
0-5 mm. PD	6		5		11	
6-10 mm. Merck		1.5		2.7		1.9
6-10 mm. PD	32		12		44	
11-20 mm. Merck		8.3		6.7		7.7
11-20 mm. PD	11		6		17	
21 mm. or over Merck		2.9		3.4		3.0
TOTAL	388	100	181	100	569	100

TABLE 3—COMPARISON BETWEEN DEGREE OF INDURATION

Parke, Davis 48 hr. & 72 h. — Merck 48 h. & 72 h.

Degree of Change In Induration	Parke, Davis						Merck					
	White		Negro		Total		White		Negro		Total	
	No.	per cent	No.	per cent	No.	per cent	No.	per cent	No.	per cent	No.	per cent
48 h and 72 h agree within bracket	302	78	134	73.6	426	75.0	290	75.0	150	82.4	440	79
21 mm. or over 48 h	22		10		32		27		12		39	
11 mm. to 20 mm. 72 h		5.7		5.5		5.7		7.0		6.6		6.8
11 mm. to 20 mm. 48 h	46		22		68		52		12		64	
6 mm. to 10 mm. 72 h		11.9		12.0		12.0		13.5		6.6		9.9
6 mm. to 10 mm. 48 h	10		6		16		9		3		12	
0 mm. to 5 mm. 72 h		2.6		3.3		3.1		2.3		1.7		1.9
0 mm. to 5 mm. 48 h			1		1		1		1		2	
6 mm. to 10 mm. 72 h				0.4		0.4		0.2		0.5		0.3
6 mm. to 10 mm. 48 h	7		7		14		6		1		7	
11 mm. to 20 mm. 72 h		1.8		3.8		2.9		1.5		0.5		1.0
11 mm. to 20 mm. 48 h			2		2		2		3		5	
21 mm. or over 72 h				0.9		0.9		0.5		1.7		1.1
TOTAL	387	68	182	32	569	100	387	68	182	32	569	100

11 mm. or over in 89.4 per cent of the 47 patients in this bracket. So far as race is concerned Table 5 reveals that few negroes with proved pulmonary tuberculosis had indurations of less than 11 mm. and in each age group with the exception of two the degree of reaction in the negro was larger than in the white. In 82.9 per cent of the white patients the degree of induration was greater than 10 mm. whereas in 87.0 per cent of the negro patients the degree of induration was greater than 10 mm.

Discussion

Seven patients (1.2 per cent of our cases) with proved pulmonary tuberculosis were negative to both intermediate PPD and O.T. but were positive to second strength PPD. It can be concluded, therefore, that so far as diagnosis is concerned second strength PPD is reliable as an exclusion test for clinical pulmonary tuberculosis. On the other hand, a negative intermediate PPD alone does not rule out clinical tuberculosis. It can also be stated that a positive skin test does not mean that clinical tuberculosis is present, nor does it mean that a person has been infected with tubercle bacilli. Individuals with atypical acid-fast bacilli infection often react positively to commercial PPD. If the initial skin test to intermediate PPD proves to be negative the test should always be repeated since technical error may account for the negative test. On re-testing 15 patients (2.6 per cent) in this series, the cases which had been positive to one brand of tuberculin and negative to the other at the time of the first tests, all were found to be positive to both tuberculins. Because two skin tests were performed simultaneously in all our cases, the one test was a check on the other and the two tests acted in effect as re-tests in all the cases. Where the intermediate PPD test proved negative and the O.T. test of similar strength was positive the patient was considered to be infected with acid-fast bacilli. Since 10 of our patients with proved pulmonary tuberculosis were negative to intermediate PPD, but positive to O.T., it is important to use this test in all such cases. Otherwise proved cases of clinical tuberculosis would be missed if intermediate PPD alone were being used as a diagnostic test.

Seibert states that the results of her experiments suggest that PPD and O.T. are qualitatively different. In addition to the presence of non-specific substances in O.T. it is possible that the two tuberculins have different antigens with different specificities, but they may also have different proportions of some of the same antigens. She further points out that reactions are frequently missed altogether with one of the test suubstances and this almost never occurs when the same or similar tuberculins are compared. This has been true in our series of cases. The results as given by Seibert indicate that different antigens are exerting their effects in people with different sensitivities. The above explanations might be applied to the 10 cases in our series which were negative to PPD but positive to O.T.

Seibert has also pointed out that PPD possesses the advantage of being less variable in potency than commercial O.T. and it is less likely to produce false reactions on repeated tests because the bacilli in its preparation are grown on protein-free synthetic medium.

Definite differences in the degree of reaction to the two commercial tuberculins used in this study have been demonstrated. It has been shown, however, that when one tuberculin test was positive the other brand tuberculin produced a positive test in all cases. It is concluded that differences in the manufacture of the two tuberculins are not significant so far as diagnosis is concerned.

It has been shown also that the size of the indurations produced by the two tuberculins at 48 hours and 72 hours showed no change in a little less than half of the

TABLE 4—CHANGE IN INDURATION IN MILLIMETERS
48 to 72 Hours

	Merck			Parke, Davis		
	No.	per cent		No.	per cent	
TOTAL NUMBER OF CASES	569	100.0		569	100.0	
No Change	270	47.4		275	48.4	
Decrease	231	40.6	2.9 mm.	234	41.7	3.2 mm.
Increase	68	12.0	3.2 mm.	60	10.5	3.0 mm.

CHANGE IN INDURATION AT 48 HOURS
Merck and Parke, Davis

TOTAL NUMBER OF CASES	569	100.0	
No Change	302	53.0	
Merck Greater	179	31.5	3.6 mm.
Parke, Davis Greater	88	15.5	3.7 mm.

TABLE 5—SIZE OF REACTION TO INTERMEDIATE PPD or O.T. IN RELATION TO AGE AND RACE

Years	1 - 5 mm.						6 - 10 mm.						11 - 20 mm.						21 mm. or over						TOTAL	
	White		Negro		Total		White		Negro		Total		White		Negro		Total		White		Negro		Total			
	No.	per cent	No.	per cent	No.	per cent	No.	per cent	No.	per cent	No.	per cent	No.	per cent	No.	per cent	No.	per cent	No.	per cent	No.	per cent	No.	per cent	No.	per cent
11.20	1	14.3			1	5.0	1	14.3	2	15.4	3	15.0	5	71.4	7	53.9	12	60.0			4	30.7	4	20.0	20	4.0
21-30							6	22.2	2	8.3	8	15.7	16	59.2	14	58.3	30	58.8	5	18.5	8	33.2	13	25.5	51	10.2
31-40			1	3.5	1	0.9	13	17.8	2	6.9	15	14.7	43	58.9	20	69.9	63	61.8	17	23.3	6	20.7	23	22.5	102	20.4
41-50	5	6.3	1	2.2	6	4.7	10	12.5	6	12.7	16	12.6	52	65.0	33	70.2	85	67.9	13	16.2	7	14.9	20	14.8	127	25.4
51-60	3	5.3			3	3.6	7	12.3	3	11.5	10	12.0	37	64.9	19	73.1	56	67.4	10	17.5	4	15.4	14	16.8	83	16.6
61-70	2	3.6	1	7.1	3	4.3	6	10.7	2	14.3	8	11.4	35	62.5	9	64.3	44	62.8	13	23.2	2	14.3	15	21.4	70	14.0
71 and over							4	10.2	1	12.5	5	10.6	24	61.5	6	75.0	30	63.9	11	28.3	1	12.5	12	25.5	47	9.4
TOTAL	11	3.2	3	1.9	14	2.8	47	13.9	18	11.1	65	13.0	212	62.5	108	67.0	320	64.0	69	20.4	32	20.0	101	20.2	500	100.0

cases. In over 40 per cent of the cases the size of the indurations was greater at 48 hours than at 72 hours and in over 10 per cent of the cases the reactions to both brands of tuberculin were larger at 72 hours than at 48 hours. From a practical standpoint a reading at 48 hours would have been sufficient in this group of cases.

From this study it may be concluded also that the average size of the indurations produced by the two intermediate tuberculin tests were greater in the negro than in the white. It may be further stated that fewer negro patients than white patients with proved tuberculosis have indurations of less than 11 mm. in diameter. Since 2.8 per cent of this series of cases of proved clinical tuberculosis had induration of less than 6 mm. in diameter it is concluded that any induration, no matter how small, is significant and should be considered as diagnostic of the presence of acid-fast bacilli.

The majority of the patients in this series was over 40 years of age. As has been shown the great majority of patients showed reactions larger than 10 mm. in diameter. Surprisingly the very old had indurations greater than the other age groups including the very young. In the years when the population of our tuberculosis hospitals was made up largely of young people with active clinical tuberculosis we saw fewer old people with active disease. Many of these old people had smaller tuberculin reactions than was seen in the young because of the fact that tubercle bacilli were not multiplying in their lesions and because degenerative forms were present. The rate of mulitplication of bacilli in the body definitely affects the allergic response to tuberculin. Today tuberculosis in the aged is usually associated with active multiplication of bacilli in their lesions. This probably accounts for the very active response to the tuberculin tests in this group. Since only 4.0 per cent of the cases were in the very young group in this series and only 9.4 per cent in the very old no definite conclusions can be made as to why these differences occurred.

SUMMARY

This study was undertaken to determine the role of intermediate and second strength PPD in the diagnosis of tuberculosis and in addition, to determine if possible whether there might be any differences in the manufacture of PPD. Two commercial brands of PPD were used, one being given on the volar surface of one forearm and one on the other.

If these tests were negative, the same strength intermediate OT was given and if the patient again failed to react, a second strength PPD was given. The degree of induration was measured at 48 hours and at 72 hours under four headings, namely, 0 mm. to 5 mm., 6 mm. to 10 mm., 11 mm. to 20 mm., and 21 mm. or over.

Seven (1.2 per cent) of the cases reacted only to second strength PPD. So far as diagnosis is concerned, a second strength PPD is reliable as an exclusion test for tuberculosis; however, a negative intermediate PPD does not rule out tuberculosis. Although there were definite differences in the degree of reaction to the two commercial tuberclins, when one was positive the other was always positive. These differences in reaction are therefore not important so far as diagnosis is concerned.

ACKNOWLEDGEMENT: I wish to thank Merck, Sharp and Dohme and Parke, Davis and Company for supplying some of the tuberculin used in this study.

RESUMEN

Se ha emprendido este estudio para determinar el papel de la dosis intermedia y segunda de potencia del PPD en el diagnóstico de la tuberculosis y además para determinar en lo posible si podría haber alguna diferencia en la manufactura del PPD. Dos productos comerciales se usaron siendo usada una en la superficie anterior del antebrazo y la otra en el otro antebrazo.

Si las dos pruebas resultaban negativas, se usaba la misma dosis intermedia de OT y si el enfermo aún no reaccionaba, se daba el PPD de potencia aumentada de PPD.

El grado de induración se midió a las 48 horas y a las 72 horas bajó cuatro rubros: de 0 a 5 mm.; de 6 a 10 mm.; de 11 a 20 mm. y de 21 o mas mm.

Siete (1.2 por ciento) de los casos reaccionaron sólo a la dosis segunda de PPD. En lo que se refiere al diagnóstico una segunda potencia en la dilución de PPD es de fiar como prueba de exclusión para tuberculosis; sin embargo, una dosis intermedia de PPD no descarta la tuberculosis. Aunque hubo definidas diferencias en el grado de reacción en las dos tuberculinas comerciales, cuando una fué positiva la otra fué siempre positiva. Las diferencias en la reacción son hasta ahora sin importancia para el dignóstico.

RESUMÉ

Cette étude fut entreprise pour déterminer le rôle de la tuberculine purifiée de concentration moyenne et de concentration numéro 2 dans le diagnostic de tuberculose et pour déterminer en outre, si possible, s'il y avait quelque différence dans la qualité de ce produit. Deux types commerciaux de tuberculine purifiée furent utilisés, l'un étant donné sur la face interne d'un des avant-bras, l'autre sur l'autre.

Si ces tests étaient négatifs, le même était recommencé à une concentration intermédiaire et si le malade ne réagissait pas, la tuberculine de concentration n°2 était

utilisée. Le degré d'induration fut déterminé après 48 heures et 72 heures selon quatre degrés: de 0 à 5 mm.; de 6 à 10, de 11 à 20 et de 21 mm. et plus.

Sept des cas étudiés (1.2%) ne réagirent qu'à la tuberculine de concentration n°2. En ce qui concerne le diagnostic la tuberculine purifiée à la concentration n°2 est un test certain d'exclusion de la tuberculose; la négativité de la réaction à la tuberculine de concentration moyenne n'exclut pas la tuberculose. Bien qu'il y eut des différences nettes dans l'importance des réactions aux deux tuberculines du commerce, lorsque l'une était positive, l'autre l'était toupar conséquent quand elles ne sont utilisées que pour le diagnostic.

ZUSAMMENFASSUNG

Diese Untersuchung wurde unternommen zwecks Bestimmung der Rolle der intermediären und zweiten Stärke von PPD bei der Diagnose der Tuberkulose und darüber hinaus, um, wenn möglich, festzustellen, ob etwa irgendwelche Abweichungen in der Herstellung von PPD auftreten. Zwei im Handel befindliche Sorten von PPD wurden benutzt; die eine von beiden an der Innenfläche des einen Unterarmes und die zweite an der anderen angewandt.

Waren diese Proben negativ, wurden dieselbe intermediare Stärke von Alttuberkulin verabfolgt, und falls der Patient auch darauf wiederum nicht reagierte, eine zweite Stärke von PPD gegeben. Der Grad der Induration wurde nach 48 Stunden und nach 72 Stunden gemessen und nach 4 Größenordnungen bestimmt, nämlich von0, 0 bis 5 mm, von 6 - 10 mm, von 11 - 20 mm und von 21 mm und mehr.

Sieben (1.2%) Fälle reagierten nur auf die zweite Stärke von PPD. Was die Diagnose angeht, so ist eine zweite Stärke von PPD glaubwürdig als Test zum Ausschluß einer Tu erkulose; eine negative Reaktion bei intermediärer Dosis von PPD schliesst dagegen die Tuberkulose nicht aus. Obwohl eindeutige Unterschiede bestanden im Ausmaß der Reaktion zwischen den beiden kommerziellen Tuberkulinen, so war doch auch die Reaktion auf das andere Präparat positiv, wenn dies bei dem einen der Fall war. Diese Unterschiede in der Reaktion sind demnach nicht von Bedeutung, wenigstens was die Diagnostik angeht.

REFERENCE

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Hypertrophic Osteoarthropathy in Association with Pulmonary Metastases from Extrathoracic Malignancies*

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Hypertrophic pulmonary osteoarthropathy, or Marie-Bamberger disease, was first described by Eugen von Bamberger[2] in 1889 and then by Pierre Marie[25] in 1890. In the intervening years, it has become widely recognized, and a number of monographs have been published on the subject.[3,11,13,24,34,35,39] It appears almost always with clubbing of the fingers and toes. The latter is synonymous with Hippocratic fingers, although Hippocrates,[12] in his original concept, described only a curving of the nails associated with empyema. This pathologic condition has been observed over the centuries. Yet, today, though clubbing occurs much more often than does hypertrophic osteoarthropathy, it is the latter which is the more frequently discussed in the literature. The clinician is cognizant of the importance of both.

That primary carcinoma of the lung can cause clubbing and osteoarthropathy is well known because of the frequency of their occurrence, but that patients with pulmonary metastases from extrathoracic malignancies can manifest these conditions is not so well known because of the rarity thereof. The following case report is an example of this unusual occurrence. It initiated a search of the literature for similar cases.

M.G., a white man, 57 years of age, who had had mild diabetes for many years, was first seen at Doctors Hospital, New York City, on April 10, 1957, because of roentgenographic evidence of a round shadow in the middle lobe of the right lung. The past history was of import in that he had had a tumor removed from the musculature of the left arm in 1955. It had been known to be present for some time prior to excision. On pathologic examination, the specimen was reported as a rhabdomyosarcoma. The patient remained well. In December, 1956, on a routine roentgenographic examination, a small infiltrate was noted in the middle lobe of the right lung. Its significance was not recognized at that time.

During the latter part of March, 1957, he developed severe "rheumatic" pains in his ankles and lower legs, and his temperature was slightly elevated. He also had a mild cough without expectoration. At that time, a roentgenogram of the chest showed a circumscribed shadow in the middle lobe of the right lung (Figure 1); he was, therefore, admitted to the hospital.

Physical examination disclosed moderate clubbing of the fingers and toes, with swelling around the ankle joints and marked tenderness over the lower tibiae. There was a well-healed scar on the left arm, without evidence of recurrence. Roentgenographic examination of the long bones did not show any definite evidence of periostitis, but the signs and symptoms were characteristic of hypertrophic osteoarthropathy.

The pulmonary shadow had the distinctive appearance of a malignant neoplasm. Was it a primary or a metastatic tumor? We had never seen nor heard of, a pulmonary metastasis complicated by hypertrophic osteoarthropathy. Furthermore, none of our colleagues had ever seen such an occurrence. We felt that we were dealing with a "second primary." Primary or secondary, an exploratory thoracotomy was indicated.

On April 16, right thoracotomy was performed and a tumor was found in the middle lobe. There was no evidence of hilar or mediastinal node involvement and the upper and lower lobes were normal. The middle lobe, which had complete fissures between it and the other lobes, was resected. Pathologic examination of the specimen proved it to be a metastatic rhabdomyosarcoma, quite similar in cell structure to the original tumor.

*Presented at the 25th Annual Meeting, American College of Chest Physicians, Atlantic City, June, 1959.

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As is so characteristic, the pains in the ankles and legs disappeared within 48 hours after operation; the clubbing of the fingers regressed slowly and had practically disappeared by March, 1958, at which time the patient felt well.

In August, he noted a feeling of malaise and occasionally expectorated blood-streaked sputum. The pains in the ankles and legs recurred, and he again noted a change in the contour of his finger tips. On roentgenographic examination of the chest, a large circumscribed shadow was seen in the upper lobe of the left lung (Figure 2). Again the chief complaint was the bone and joint pains. It was felt that there was a second metastatic tumor in the left lung and resection was indicated. He was readmitted to the hospital. Physical examination showed moderate clubbing of the fingers and toes, and the ankles and lower tibiae and fibulae were exquisitely tender. The diabetes was mild and easily controlled.

On October 23, left thoracotomy was performed. A circumscribed tumor mass, similar to the one removed from the right lung, was found in the upped lobe. It was removed by wedge resection in order to preserve as much pulmonary tissue as was possible. Pathologic examination of the specimen proved it to be a second metastatic rhabdomyosarcoma. Once again the pains in the ankles and long bones disappeared within a few days after operation, and the patient made an uneventful recovery. When last seen in December, 1958, he felt well and had no pains in his legs, but the clubbing was still present, albeit less marked.

In reviewing the literature, we found that a number of authors[25,30,39,44] have made passing reference to the association of hypertrophic osteoarthropathy with pulmonary metastases from extrathoracic malignancies, but only 28 such cases have been reported since it was first described by von Bamberger in 1889 (Table 1).

The incidence of hypertrophic osteoarthropathy in primary carcinoma of the lung differs greatly in various reports. This may be due to the selection of the cases in some of the series. Jack[21] found clubbing in 40 per cent and hypertrophic osteoarthropathy in 1.2 per cent of 668 patients. In a series of 959 patients with bronchogenic carcinoma seen at The Mount Sinai Hospital, New York City, 255 (26 per cent) developed clubbing, but only seven (0.73 per cent) had clinical symptoms of hypertrophic osteoarthropathy.[1] Semple and McCluskie[38] believe the incidence of osteoarthropathy to be from 1 to 2 per cent, and Flavell[14] states that it is about 2 per cent. Weiman et al,[45] of the Mayo Clinic, reported that of 481 patients with resectable bronchogenic carcinomas, 25 (5.2 per cent) had hypertrophic osteoarthropathy, and that of 14 patients with resectable pleural mesotheliomas, it occurred in eight (57.1 per cent). Ray and Fischer[33] found 14 cases of osteoarthropathy in 139 patients with primary carcinoma of the lung. Of these 14, all but one were peripheral type

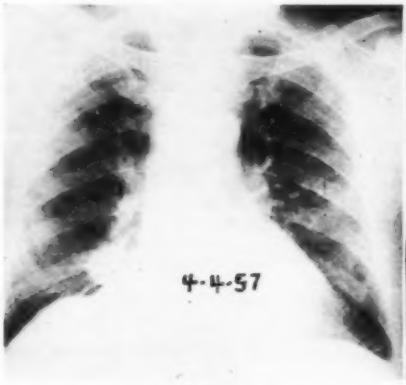

FIGURE 1

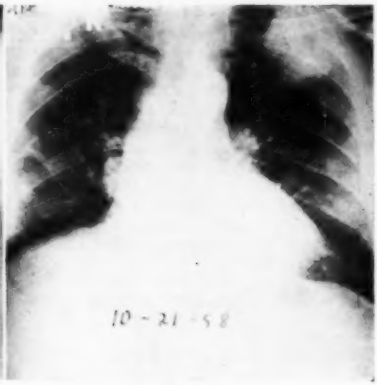

FIGURE 2

neoplasms. Hansen,[18] reporting a series of 100 bronchogenic carcinomas, cited 12 patients with Marie-Bamberger disease.

In order to attempt to determine the incidence of clubbing and hypertrophic osteoarthropathy in patients with pulmonary metastases from extrathoracic malignancies, the records of such patients at Montefiore Hospital, New York City, were examined. A total of 883 charts and postmortem records were reviewed. Clubbing was recorded in only 34 cases (3.8 per cent). There was none with clinical symptoms of hypertrophic osteoarthropathy. Roentgenographic bone surveys were made in many of these patients in a search for osseous metastases. In one, there was a periostitis suggestive of hypertrophic osteoarthropathy. It cannot be asserted that the patient with pulmonary metastases does not live long enough to develop clubbing or osteoarthropathy because many of them had evidence of pulmonary metastases months before they came under observation or to post mortem. Of those cases in which the duration of the metastases could be determined, we found that they had been present for more than three months in over 50 per cent of the patients and for more than one year in 10 per cent.

It has been observed that hypertrophic osteoarthropathy occurs more frequently with the peripheral circumscribed type of bronchogenic carcinoma than with the hilar or main bronchus tumor.[33,36] It is also not uncommon to find that when hypertrophic osteoarthropathy regresses following the removal of a primary carcinoma of the lung, it may reappear when pulmonary metastases occur.[13,30] Contrariwise, pulmonary

TABLE 1 — TWENTY-EIGHT CASES PREVIOUSLY REPORTED

Author	Year	Primary Site	Pathology
Virchow[42]	1895	Humerus	Chondrosarcoma
Cotteril[10]	1901	Femur	Sarcoma
Hall[17]	1905	Femur	Sarcoma
Kruger[22]	1906	Breast	Carcinoma
Oliver[29]	1918	Femur	Sarcoma
Hoffman[19]	1919	Uterus	Carcinoma
Weinberg[43]	1919	Femur	Sarcoma
Bryan[7]	1920	Forearm	Sarcoma
Bryan[8]	1925	Knee	Sarcoma
Rijkmans[35]	1928	Breast	Carcinoma
		Tonsil	Carcinoma
Crump[11]	1929	Breast	Carcinoma
Blumensaat[6]	1931	Skin	Melanocytoblastoma
Morales-Gonzalez[28]	1933	Not given	Sarcoma
Palugyay[31]	1934	Femur	Sarcoma
Rypins[36]	1935	Groin	Fibrosarcoma
Penitschka[32]	1938	Tibia	Sarcoma
Barta[4]	1939	Femur	Sarcoma
Tobler[40]	1939	Uterus	Sarcoma
Van Hazel[41]	1940	Abdominal Wall	Fibrosarcoma
Benard et al[5]	1943	Uterus	Carcinoma
Kollbrunner[23]	1948	Fibula	Sarcoma
Bariety and Coury[3]	1950	Kidney	Carcinoma
		Kidney	Carcinoma
		Uterus	Chorioepithelioma?
Holmes et al[20]	1950	Tendon (hand)	Giant Cell Tumor
Ray and Fischer[33]	1953	Not given	Fibrosarcoma
Garcia De Lima[16]	1955	Not given	Myxochondrosarcoma

metastases from extrathoracic malignancies, even though peripheral, circumscribed, and usually multiple, rarely cause hypertrophic osteoarthropathy.

The high percentage of sarcomas in the metastatic pulmonary malignancies producing hypertrophic osteoarthropathy (Table 1) lends credence to the theory of Mendlowitz,[27] namely, that vascular pulmonary tumors cause an increase in the pulmonary circulation and thereby produce the increased digital blood flow which in turn causes the pathologic changes. Sarcomas are vascular tumors. Primary sarcomas of the lung are rare but they, too, have been reported in association with hypertrophic osteoarthropathy.[2,37]

When a solitary neoplasm develops in the lung following resection of a malignancy, either intra- or extra-thoracic, the differential diagnosis between a metastasis and a "second primary" is always a problem. Should clubbing and hypertrophic osteoarthropathy also occur, one cannot rule out the possibility that the pulmonary neoplasm might be metastatic, especially if the original tumor were a sarcoma.

SUMMARY

A case report of a patient who developed clubbing and symptoms of hypertrophic osteoarthropathy with each of two metachronous, metastatic, pulmonary rhabdomyosarcomas is presented. The metastases were resected; there was an interval of 18 months between the operations, and the symptoms regressed after each procedure. Only 28 cases of hypertrophic osteoarthropathy associated with pulmonary metastases from extrathoracic malignancies have been reported in the literature. Seventeen of these neoplasms were sarcomas. In a series of 883 patients with pulmonary metastases from extrathoracic malignancies, 34 (3.8 per cent) had clubbing and none had clinical symptoms of hypertrophic osteoarthropathy.

RESUMEN

Se relata el caso de un enfermo que presentó dedos hipocráticos síntomas osteoartropatía hipertrófica con cada una de dos metástasis pulmonares de rabdomiosarcomas.

Se resecaron las metástasis; hubo uun intervalo de 18 meses entre las operaciones y los síntomas retrocedieron después de cada operación. Sólo 28 casos de osteoartropatía hipertrófica en asociación con metástasis pulomnares de neoplasias malignas extratorácicas se han publicado. Diecisiete de estas neoplasias fueron sarcomas. En series de 883 enfermos con metástasis pulmonares de neoplasias malignas extratorácicas 34 (3.8 por ciento) tenían dedos hipocráticos y ninguno tenía síntomas de osteoartropatía hipertrófica.

RESUMÉ

L'auteur présente l'observation d'un malade atteint d'hippocratisme digital et d'ostéo--arthropathie hypertrophiante avec pour chacune de ces manifestations l'association d'une métastase pulmonaire ed rhabdomyosarcome. Les métastases furent enlevées; il y eut une période de 18 mois entre les opérations, et les symptômes régressèrent après chaque opération. 28 cas seulement d'ostéo-arthropathie hypertrophiante, associée à des métastases pulmonaires provenant de cancers extra-thoraciques ont été rapportés dans la litérature. 17 de ces néoplasies étaient des sarcomes. Dans un groupe de 883 malades, atteints de métastases pulmonaires de cancers extra-thoraciques, 34 (3.8%) eurent un hippocratisme digital et aucun n'eut de symptômes cliniques d'ostéo-arthropathie hypertrophiante.

ZUSAMMENFASSUNG

Es wird eine Krankengeschichte eines Patienten mitgeteilt, bei dem Trommelschlegelfinger auftraten sowie Symptome iner hypertrophierenden Osteoarthropathie mit zwei metastatischen pulmonalen Rhabdomyosarkomen. Diese Metastasen wurden reseziert; zwischen den Operationen lag ein Intervall von 18 Monaten, und die symptome bildeten sich nach jedem Eingriff zurück. In der Literatur sind bisher nur 28 Fälle von hypertrophierender Osteoarthropathie in Verbindung mit Lungen-metastasen extrathorakaler bösartiger Tumoren mitgeteilt worden. 17 dieser Neoplasmen waren Sarcome. In einer Reihe von 883 Kranken mit Lungenmetastasen extrathorakaler bösartiger Geschwülste hatten 34 (3.8%) Trommelschlegelfinger, und keiner hatte klinische Symptome einer hypertrophierenden Osteoarthropathie.

Complete reference list will be published in the reprints

Postoperative Empyema: Etiology, Prevention and Treatment*

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In considering pulmonary resection, a study of the literature and an observation of patients make it evident that the extent of lung tissue removed will influence the mortality rate, the incidence of morbidity, and the type of complications. Therefore, a survey of pulmonary resections should be divided into three classifications: pneumonectomy, lobectomy, and segmental and/or wedge resections.

In the discussion of postoperative empyema, pulmonary resections should be divided into two major groups, (a) pneumonectomy, in which all lung tissue on one side is removed, and (b) pulmonary resections involving less than the entire lung. In the latter procedure the simple effective principle of obtaining an expanded lung and an empty or obliterated pleural space can be achieved. In lobectomy or segmental resection, as long as the remaining lung is expanded it is an effective respiratory organ and a space-occupying mass. By expansion of the remaining lung tissue, by narrowing of the intercostal spaces, by elevation of the diaphragm, and by shifting of the mediastinum the pleural space is obliterated or emptied of air, fluid, or other material. Free surfaces are eliminated. There is intimate contact between the expanded lung and the tissues that make up the wall of the pleural cavity. With the elimination of free surfaces bacteria that may be present are directly under the influence of inflammatory reaction, and, if present in the blood stream, antibodies, antibiotics, and chemotherapeutic agents are brought to the region of inflammation by the blood stream. Whether or not the amputated and sutured bronchial stump is covered by pleura or other living tissue is relatively unimportant, since obliteration of the pleural space will effectively surround the amputated closed bronchus by living tissue. In pneumonectomy, pleural space infection or pleural empyema is more likely to occur and it is a much more serious complication because there is no remaining lung tissue to expand on the operated side to obliterate the pleural space. If bacteria are present they have the advantage of growing in a fluid medium and of attacking a free surface. When bacteria are present upon or attack a free surface area they are not within living tissue. This gives them a great advantage over the body for they are outside the effectiveness of the nonspecific inflammatory reaction.[31] Similarly, since the bacteria are not within living tissue or surrounded by living cells they are outside the effective range of antibodies, antibiotics, and chemotherapeutic agents that can, if present in the blood stream, be brought into and concentrated in the tissues about the site of bacterial invasion. In pneumonectomy the amputated sutured bronchial

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stump, if not retracted into the mediastinum or deliberately covered by pleura or other living tissue, is in reality a free surface exposed in the pleural cavity.

The discussion in this presentation is based upon a review of the literature and the study and analysis of 320 consecutive resections of all types performed by the senior author, in addition to 63 consecutive pneumonectomies at the Baltimore City Hospitals during the years 1941 to 1954 inclusive. The same general operative technics were employed in all surgical procedures. The indications for surgery, preoperative management, and general outline of postoperative care were practically the same in all patients.

Table 1 is a summary of the complications of bronchopleural fistula and empyema following pneumonectomy as reported by various authors. In the series being reported here, as shown in Table 2, there was a total of 11 true bronchopleural fistulas in a total of 383 resections, (2.8 per cent). Of these eleven, two were found following pneumonectomy for carcinoma, three after pneumonectomy for tuberculosis, one after lobectomy for tuberculosis, four after lobectomy for lung abscess, and one after lobectomy for bronchiectasis. There were four broncho-alveolo-pleural fistulas following lobectomies and segmental resections for tuberculosis. None of these required secondary surgery.

There was a total of 13 (3.4 per cent) empyemas without bronchopleural fistula in the entire series. Of these 13, four developed after pneumonectomy for carcinoma, four following pneumonectomy for tuberculosis, one after lobectomy for lung abscess, three after pneumonectomy for bronchiectasis, and one after segmental resection for the same disease. There were only two (1.3 per cent) instances of empyema without bronchopleural fistula after lobectomy or segmental resection. It is interesting to observe that of 13 cases of empyema, eleven (4.8 per cent) developed after pneumonectomy, which again emphasizes the unfavorable conditions for infection prevailing in these patients.

The etiology of empyema after pulmonary resection is bacterial. The source of bacteria can be traced to preoperative infection of the lung parenchyma, the bronchus, the lymphatic vessels or glands, the pleura, or the chest wall. The type of bacteria causing infection depends upon the type of infection present before operation. Rarely does it result from outside contamination. The infection may be caused by an inadvertent break into an infected area of lung tissue or by a spill of infected material from the divided bronchus. It may also result from failure to remove any pleura that was infected before the operation.[28] Faulty closure, failure of wound healing, or continued progression of the disease in the bronchial stump may lead to leakage of the bronchial stump with fistula into the pleural cavity, thus causing empyema. Tube drainage of the pleural cavity may be a portal of entry for bacteria that will cause infection of the pleural cavity. This is of great importance when considering empyema after pneumonectomy. In two patients a superficial wound

infection ulcerated into the pleural cavity, causing empyema by contamination from the outside. The infection is usually of a mixed pyogenic type but it may be a pure culture type, especially in tuberculous empyema after resection for pulmonary tuberculosis.

The prevention of pleura empyema after pulmonary resection resolves itself into the recognition of the etiologic factors and a carefully planned method of avoiding these factors as far as possible. Since the general wellbeing of a patient affords better resistance to infection, he should be brought into as good condition as possible before operation. Anemia, if present, should be corrected by blood transfusions. Protein deficiency should be corrected. Any concomitant illness, such as diabetes mellitus, must be brought under control. When possible it is always desirable to eliminate or bring under control all infection of the tracheobronchial tree, lung, and pleura before operation. Usually this can be accomplished by the correct preoperative preparation of the patient by means of a specific antibiotic or chemotherapy agent. Although there may be no infection before operation it is desirable to administer a broad spectrum antibiotic agent or combination of agents for 24 to 48 hours before operation. Proper preparation of the skin at the operative site is important. Shaving of the area hours before operation is to be avoided since it permits the multiplication of bacteria in small abrasions or cuts in the skin caused by the razor.

At the time of operation care should be taken to prevent the inadvertent opening of infected lung tissue. It can be accomplished best by extrapleural dissection of all areas where the lung is adherent. Infected pleura always should be removed. Although treatment of the bronchial stump is not part of the subject under discussion, it is such an important causative factor of empyema that it must be discussed. A spill of infected secretions from the divided bronchial stump should be avoided. This is accomplished best by using a closed technic, that is, dividing the bronchus between clamps and applying one layer of sutures before removal of the clamp on the proximal bronchus. If the open method is used, great care must be taken in aspirating and the anesthetist should be warned of the open bronchus so that he will not force tracheobronchial secretions into the pleural cavity through the open divided bronchial stump. In pneumonectomy, since the condition of the bronchus is known before operation as shown by bronchoscopy and since the bronchus can be palpated so readily at the time of operation, there is nothing to be gained by the open method. The prevention of bronchial fistula must always be considered as the bronchus is being prepared for amputation. It should not be stripped completely of surrounding tissue unless absolutely necessary, nor should it be divided through diseased tissue.[23] The bronchial stump is made short and merely long enough to permit adequate suturing. It should be carefully sutured with nonabsorable sutures. Obviously, the method of suturing the amputated bronchus is not too important so long as a nonabsorable suture material is used. The same

method of suturing the amputated bronchus has been used throughout the present series. For pneumonectomy it consists of two rows of interrupted mattress sutures and a row of simple interrupted sutures over the crushed end of the bronchial stump.[9,20] For resections less than pneumonectomy it consists of a single row of mattress sutures and a row of simple interrupted sutures over the crushed end of the bronchial stump. The bronchus is deliberately crushed with a clamp and the crushed end is not excised since by examination of available early autopsy material it is evident that the crushed tissue promotes the healing. Unless injured, as by crushing, mucous membrane surface will not heal to mucous membrane surface. The mattress sutures function as stay sutures. In all cases without exception where pneumonectomy was done, living tissue was used to cover the amputated sutured bronchial stump. It is true that in some instances this objective is more easily and adequately accomplished than in others. The necessity of such a method is supported by many workers.[1,3,5,9,11,12,24,25,26] The efficiency of surrounding a potential leaking point by living tissue is supported by its use in general surgery. The amputated sutured duodenal stump is buried into the pancreas or other living tissue. Brewer[5] has described a satisfactory method of obtaining a pedunculated living graft. Usually tissue in the vicinity of the bronchial stump can be obtained. The esophagus is always available. It has been used on many occasions in this series of patients and never has there been esophageal obstruction, perforation, or fistula. Therefore, it is well to repeat and emphasize that the best treatment for bronchopleural fistula after pneumonectomy is to prevent its occurrence by covering the sutured bronchial stump with living tissue.

When less than the entire lung is removed it is not so important to cover the amputated sutured bronchial stump with living tissue. Some lobar and many segmental bronchial stumps are left uncovered since the surrounding lung parenchyma, in cases where expansion of the lung is not obstructed, readily covers the bronchial stump and acts as a protective barrier. This difference does not change the need for careful technic in closing any cut bronchus regardless of its size.

The use of silk or a nonabsorbable suture material throughout the operation for sutures and ligatures reduces the probability of infection. Careful hemostasis also reduces the chances of infection by preventing blood clots and hematoma. It is important to employ a sterilizing agent in the pleural cavity at the completion of the operation. Since 1942 the authors have used routinely a combination of sulfanilamide, 3 to 5 grams, and sodium tetradecyl sulfate 1:500 in azochloramide 1:3000 (200 to 500 cc.) in the pleural cavity.[2,20] It is a good nonspecific antiseptic agent and apparently reduces pleural exudation. Where there is gross contamination of the pleural space at operation caused by breaking into an infected area of lung a pulmonary abscess or preoperative empyema, or where the bronchial stump spills a cubic centimeter or more of secretions into the pleural cavity, the sulfanilamide, 5 grams, and sodium

tetradecyl sulfate 1:500 in azochloramide 1:3300 (500 cc.) mixture is instilled into the pleural cavity. The chest is closed without drainage. Each day thereafter the pleural cavity is aspirated and the mixture instilled. This is done at least three times or until three daily negative cultures are obtained. Streptomycin and penicillin are used parenterally but not instilled into the pleural cavity. In 29 consecutive patients who had gross contamination of the pleural cavity at the time of pneumonectomy, empyema occurred in only one instance, the sixth of the series. Because of antibiotic sensitivity this patient was not able to tolerate antibiotics of any sort before or after operation. It is apparently easier to kill bacteria before they have had the opportunity to invade the tissues and set up true infection or empyema. Indeed it is a great comfort to know that gross contamination of the pleural space need not result in empyema.

The authors do not drain the pleural cavity after pneumonectomy because of the possibility that the drainage tube may act as a portal of entry for bacteria. However, in resection less than pneumonectomy, the pleural space is drained routinely by a large tube, No. 30 to 32 French, in adults, which is placed and anchored laterally, and extends from the apex of the pleural cavity to the diaphragm.[3] A large tube is used because the clotting of serum or blood is less likely to occlude the tube. It is anchored to the lateral chest wall by a loose catgut suture and consequently the tube cannot inadvertently become occluded by kinking. Above all, it will prevent the incompletely expanded lung from falling on a tube lying posteriorly and sealing it off from the air or fluid-containing pleural cavity. Multiple holes are cut in the side of the tube. Active negative suction of 2.5 cm. of mercury is used routinely in the postoperative period. It is believed that an expanded lung and an obliterated pleural space will prevent empyema even in the presence of gross bacterial contamination at operation. Postoperatively, one or more broad spectrum antibiotic agents are used routinely for approximately one week.

In spite of meticulous care postoperative pleural empyema does occur occasionally. When considering this complication it is well to divide it into two groups, (a) those that develop after pneumonectomy, and (b) those that occur when less than the whole lung is removed. Both divisions should be subdivided into (a) those with bronchopleural fistula, and (b) those without bronchopleural fistula.

The presence of a fistula is suspected when the patient has empyema, expectorates bloody fluid, or develops a gradually increasing amount of subcutaneous emphysema. Definite proof lies in the expectoration of a dye injected intrapleurally or by failure to maintain a negative intrapleural pressure on aspiration. When a bronchopleural fistula has developed a definite plan of management should be undertaken. A sharp distinction must be drawn between a bronchopleural fistula after partial lung resection and a bronchopleural fistula after total pneumonectomy; whether or not intrapleural tube drainage was carried out will definitely influence the course of the complication.

When there is a large air leak in a bronchial breakdown after pneumonectomy without tube drainage, the prompt institution of a closed type of pleural drainage will prove life-saving. Where the leak of air from the bronchus is small and slow a closed type of drainage is the choice method of treatment and this should always be done before open thoracotomy is attempted. After closed drainage has been started, if the bronchial leak is small and the patient can be positioned so that the pleural contents cannot enter the fistula and be aspirated into the good lung, it is permissible to carefully instill an antiseptic solution or an antibiotic agent that is best suited for the type of bacteria found. It is advisable to use an agent that will tend to seal over the air leak and not cause a further breakdown of the bronchial stump by producing increased irritation or inflammation. Streptokinase and streptodornase or tryptar should not be used in such patients. It is believed that the best results are obtained by the use of a mixture of sodium tetradecyl sulfate 1:500 and azochloramide 1:3300 with sulfanilamide since it is a good nonspecific antiseptic agent, a mild detergent, and apparently aids the quick sealing of air leaks. When desired or where indicated a specific antibiotic agent may be added. If the air leak can be overcome and the infection prevented or eliminated, the tube may be removed. Should this conservative management prove unsuccessful it is advisable to perform an open thoracotomy. It is best to select a type that will remain open permanently. An open thoracotomy should be continued for approximately six months. Eventually the mediastinum will retract to a greater or lesser degree into the empty pleural space. The more the mediastinum retracts into the empty pleural cavity the easier will be its obliteration by thoracoplasty.

It is often an advantage to add phrenic avulsion to the management of the infected space since elevation of the diaphragm aids in obliteration of the pleural cavity. After the pleural cavity has been reduced in volume as far as possible by this method, multiple stage thoracoplasty is necessary to finally obliterate the remaining space. Usually the last stage of the operation requires some type of chest wall excision and a muscle flap transplant.[6,14,19,20] These procedures will cure the emyema and close the bronchopleural fistula. Primary closure of the bronchopleural fistula after pneumonectomy has not been undertaken by the authors and probably is unwise. By following the above plan all bronchopleural fistulas occurring after pneumonectomy have been finally and completely cured. These include the patients considered in this series as well as those first seen after bronchopleural fistula and empyema were found to be present. However, it is a long and difficult plan of treatment. It should not be undertaken for the patient with carcinoma where a recurrence or metastatic disease is anticipated.

When the entire lung has not been removed the problem of bronchopleural fistula is entirely different and definitely more amenable to treatment. One must distinguish between bronchopleural and broncho-

alveolo-pleural fistulas, since the latter usually occur while the initial drainage tube is in place and the air leak is overcome before the initial tube is removed.[3] Several methods of treatment are available where there is a true bronchopleural fistula with an opening in the amputated bronchial stump. Closed thoracotomy with [illegible] and suction as described under pneumonectomy often proves successful. The fistula and resulting empyema frequently can be remedied by a single stage thoracoplasty, particularly when the leak and empyema are in the apical region. Exploratory thoracotomy may be used in properly selected patients. The remaining lung can be freed up and a decortication done. Additional lung tissue can be resected along with the bronchopleural fistula. Murphy[20] and others concurred with this opinion. Simultaneous thoracoplasty is carried out if necessary to permit the remaining lung tissue to fill the pleural space. If the last remaining lobe is thus resected the residual pleural space can be treated by the method described for a contaminated pleural space after pneumonectomy. The chest is closed without drainage and infection may thus be avoided. Five patients in the reported series developed bronchopleural fistula after lobectomy. One required thoracoplasty to effect a cure; another was treated by transplanting a pedicle muscle flap into the bronchus and the small remaining pleural space. The others closed and were healed completely by conservative management. Other patients with bronchopleural fistula when first seen have been treated successfully by these methods.

Empyema or infection of the pleural space is diagnosed by the identification of bacteria in the pleural fluid or pus. In all cases it is necessary to rule out the presence of bronchopleural fistula. Once empyema is detected treatment must be undertaken according to the following methods: (a) sterilization of the pleural cavity by needle aspiration and instillation of antiseptics or antibiotic agents, (b) sterilization by tube drainage and instillation of the proper fibrinolytic,[22,23] antiseptic, and/or antibiotic agents, and (c) open drainage. If open thoracotomy drainage does not result in obliteration of the pleural space, it must be followed by partial thoracoplasty when less than a lung has been resected and by complete thoracoplasty after empyema following pneumonectomy. In such patients the last stage often requires some type of Schede procedure with muscle transplant. Appropriate antibiotics should be used enterally or parenterally.

Sterilization of the closed pleural space with and without pneumonectomy has been given extensive clinical trial.[4-24] Many antiseptics and mixtures of antiseptics and wetting agents, as well as many antibiotics, have been employed. Gramacidin, tyrothrycin, penicillin, streptomycin, aureomycin, chloromycetin, sulfanilamide, and mixtures of these drugs have been used. The mixtures found most effective by the authors has been azochloramide 1:3300 in sodium tetradecyl sulfate 1:500 and sulfanilamide. With daily aspiration of the pleural fluid and instillation of this mixture the infection can be controlled. It invariably results in an end

point with no bacteria found on smear but always a few colonies of hemolytic staphylococcus, either aureus or albus, found on culture. Miller[17] by experimental methods demonstrated that the addition of aureomycin to this mixture did not change the action of its various agents and did not render aureomycin ineffective. The mixture of sulfanilamide, azochloramide, sodium tetradecyl sulfate and aureomycin was then used in empyema following pneumonectomy. By daily aspirating the pleural space and instilling this mixture three cases of empyema after pneumonectomy were controlled and two of them were apparently cured. These patients were given aureomycin by mouth. The first patient thus treated finally required the drainage of a small intrapleural abscess. The drainage site healed spontaneously and thoracoplasty was not needed. The second patient had a recurrence of infection after two months. Reapplication of the treatment again promptly controlled the empyema and a negative culture resulted. The patient developed cerebral metastasis, with anaplastic carcinoma revealed by craniotomy, and died four months after the last treatment of the pleural space. The third patient was controlled promptly by needle aspiration and instillation of the mixture into the pleural space. The pleural fluid became clear and revealed no growth. The mediastinum retracted into the operated side. This patient died from metastatic carcinoma four months after the last aspiration. It cannot be determined whether empyema would have recurred. Two patients in the series were allergic to aureomycin and the treatment had to be abandoned. (There was a very limited number of antibodies available at the time of this treatment.)

Since the patient with empyema after pneumonectomy presents a more serious problem than the patient with empyema after partial lung resection, a greater effort should be made to cure empyema without surgery. If a cure is not accomplished by needle aspiration and sterilization or by administration of an appropriate antiseptic or antibiotic agent, closed tube drainage with a strict routine should be instituted. The infecting bacteria must be identified and the sensitivity of the infecting bacteria to various antibiotic agents should be determined. After an intrapleural drainage tube is inserted, the pleural cavity should be instilled through the tube once every day with one ampule of streptokinase and streptodornase in 20 cc. of distilled water, to which is added, in sufficient quantity, an antibiotic agent that is effective against the infecting bacteria or group of bacteria. This same antibiotic agent should be given by mouth or injection for its systemic effect. After the streptokinase, streptodornase, and the antibiotic agent have been placed in the pleural cavity the intrapleural tube is occluded for four hours, after which the clamp is removed and drainage allowed by the underwater seal mechanism for four hours. After this eight hour period the pleural cavity is irrigated every four hours with sodium tetradecyl sulfate 1:500 in azochloramide 1:3300 to which has been added sulfanilamide. The entire treatment must be carried out under rigid aseptic conditions. When three

successive daily intrapleural fluid cultures are found to be negative for bacteria, the intrapleural tube is removed and the tube opening closed by a single suture. The pleural cavity is aspirated by needle and instilled with sodium tetradecyl sulfate, azochloramide, and the appropriate antibiotic agent for three successive days. The pleural fluid is cultured each day. If the cultures prove to be negative the empyema will be overcome or cured. This method of treatment has been successful in three patients and has failed in two. One may use other antibiotic agents by the trial and error method. When the treatment is to be successful it will not require more than a week or 10 days. Long continued unsuccessful treatment is to be avoided. Should this method fail it will be necessary to perform an open thoracotomy followed in approximately six months by multiple stage thoracoplasty as described under bronchopleural fistula after pneumonectomy.

In the event sterilization of the empyema fails in the patient who has had less than pneumonectomy, open or tube drainage may cure the empyema. This is always true if the lung will expand and obliterate the space. If the lung will not expand to obliterate the space a limited thoracoplasty usually will suffice to obliterate the space and thus cure the empyema. In properly selected cases decortication may be treatment of choice.

SUMMARY

1. The extent of pulmonary resection determines the mortality, morbidity, and postoperative complication. Therefore, careful distinction should be made between pneumonectomy, lobectomy, and segmental resection.

2. The principle of a fully expanded lung and an empty or obliterated pleural space can be accomplished after lobectomy and segmental resection. The principle cannot be applied after pneumonectomy. Accordingly, a more meticulous sterile technic must be carried out after pneumonectomy.

3. Postoperative pleural empyema must be divided into those groups occurring after (a) pneumonectomy and (b) where less than a pneumonectomy was done. These two divisions must be further subdivided into (a) those with bronchopleural fistula and (b) those without bronchopleural fistula.

4. The best method of treatment for empyema is prevention. Means to accomplish this are described.

5. The treatment of empyema can be divided into (a) aspiration and sterilization by needle or closed thoracotomy tube method, and (b) open or closed drainage followed by thoracoplasty when needed.

RESUMEN

1. La extensión de la resección pulmonar determina la mortalidad, la morbilidad y las complicaciones postoperatorias. Por tanto, debe hacerse una cuidadosa distinción entre la necesidad de hacer neumonectomía, lobectomía y resección segmentaria.

2. El principio de un pulmón completamente expandido y espacio pleural vacío u obliterado, puede realizarse después de lobectomía y de regmentectomía. Este principio no puede aplicarse a neumonectomía. Por tanto una técnica estéril mas cuidadosa debe llevarse a cabo después de neumonectomía.

3. El empiema postoperatorio debe dividirse en estos grupos después de: (a) neumonectomía y (b) cuando menos que la neumonectomía se han hecho.

Estos dos grupos deben dividirse aún en: (a) con fístula broncopleural y (b) sin fístula broncopleural.

4. El mejor método para tratar el empiema, es la prevención. Se describen aquí esos métodos.

5. El tratamiento del empiema puede dividirse en: (a) aspiración y esterilización por aguja o tubo de toracotomía cerrado y (b) canalización cerrada o abierto seguida de toracoplastía cuando es necesario.

RESUMÉ

1. C'est l'étendue de la résection pulmonaire qui est déterminante pour la mortalité, la morbidité et les complications post-opératoires. C'est pourqui une distinction soigneuse devrait être faite entre pneumonectomie, lobectomie et résection segmentaire.

2. Une expansion pulmonaire complète et un espace pleural vide ou oblitéré peuvent être obtenus après lobectomie et résection segmentaire. Il ne peut en être de même après pneumonectomie. De même, une technique d'asepsie plus mèticuleuse doit être appliquée après pneumonectomie.

3. L'épanchement pleural post-opératoire doit être divisé en groupes survenant après (a) pneumonectomie (b) lorsqu'une résection moins importante a été faite. Ces deux divisions doivent être ultérieurement subdivisées en (a) ceux atteints de fistule bronchopleurale (b) ceux sans fistule bronchopleurale.

4. La meilleure méthode de traitement pour l'épanchement est préventive. Les moyens pour y parvenir sont décrits.

5. Le traitement de l'épanchement peut être divisé en (a) aspiration et stérilisation à l'aiguille ou tubage en thoracotomie fermée; (b) drainage ouvert ou fermé suivi de thoracoplastie si nécessaire.

ZUSAMMENFASSUNG

1. Vom Ausmaß der Lungenresektion hängen Mortalität, Morbidität und postoperative Komplikationen ab. Man muß daher sorgfältig unterscheiden zwischen Pneumonektomie, Lobektomie und Segment-resektion.

2. Das Gesetz einer im vollen Umfang ausgedehnten Lunge und eines leeren oder verödeten Pleuraspaltes kann nach Lobektomie und Segmentresektion verwirklicht werden. Das Gesetz läßt sich nicht nach der Pneumonektomie anwenden; demgamäß muß nach der Pneumonektomie eine noch sorgfältigere sterile Technik erfolgen.

3. Die postoperativen Pleuraempyeme müssen aufgegliedert werden in Grüppen, dis entstanden sind nach: (a)Pneumonektomie, (b) nach weniger ausgedehnten Eingriffen. Diese beiden Gruppen müssen weiter unterteilt werden in: (a) solche mit innerer Fistel und (b) solche ohne diese.

4. Die beste Methode zur Behandlung eines Empyems ist seine Verhütung. Mittel und Wege dies zu erreichen, werden angegeben.

5. Die Empyem-Behandlung kann aufgeteilt werden in: (a) Aspiration und Keimfreimachung mittels Punktion oder geschlossener Thorakotomie und (b) offene oder geschlossene Drainage mit anschliessender Thorakoplastik, falls erforderlich.

Complete reference list will appear in reprints.

Thioglycollate, Peroxidase, Neutral Red, Serpentine Cord, and Niacin Tests for Group Differentiation of M. Tuberculosis, Anonymous (Atypical) Acid-Fast Bacilli, and Saprophytic Mycobacteria

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In previous studies[1-3] it was observed that the thioglycollate, peroxidase, neutral red, and serpentine cord tests were useful for group differentiation of *M. tuberculosis*, atypical acid-fast bacilli, and saprophytic mycobacteria. The present investigation was undertaken to determine further the differential potential of these procedures, and to ascertain whether the niacin test[4,5] could also be used to help in the differentiation of these groups of organisms.

Materials and Methods

Fifty-five strains of recently isolated human tubercle bacilli, 45 strains of atypical acid-fast bacilli, and seven strains of saprophytic mycobacteria were selected for study. The majority of the organisms were supplied through the courtesy of other workers, as indicated.

Tubercle Bacilli: Strains A-23 through A-44 were obtained from Mr. Frank Clifton, Veterans Administration Hospital, Alexandria, Louisiana. Strains CDC-1 through CDC-3 were obtained from Dr. George P. Kubica, Communicable Disease Center, Public Health Service, Chamblee, Georgia. Strain H37Rv was obtained from Dr. William Steenken, Jr., Trudeau Laboratory, Saranac Lake, New York.

Atypical Mycobacteria: Strains AP-9, AP-10, and AS-14 through AS-16 were obtained from Mr. Frank Clifton. Strains AP-11 and AS-17 were obtained from Miss Gloria E. Veach, Veterans Administration Center, Wadsworth, Kansas.

Saprophytic Mycobacteria: Strains *M. smegmatis*-a, *M. smegmatis*-b, *M. phlei*-a, and *M. butyricum* were obtained from Dr. George P. Kubica. Strain *M. phlei*-b was obtained from Dr. William Steenken, Jr.

The tubercle bacilli and atypical organisms were isolated from various clinical specimens such as sputa, bronchial washings, gastric lavages, resected lung lesions, pleural fluids, lymph nodes, and catheterized ureteral urines. Of the 45 atypical strains, 17 were photochromogens, and 28 were scotochromogens. To avoid the use of patients' names and for convenience in arrangement, most of the strains have ben redesignated.

All the tests were performed by the methods described elsewhere[3,6] using five-week old stock cultures of Proskauer-Beck solid and Löwenstein-Jensen media. Each test was repeated three times. The final readings represent average results.

Results

The data in Table 1 summarize typical findings from each group of organisms. The thioglycollate medium failed to support the growth of

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TABLE 1 — RESULTS OF THIOGLYCOLLATE, PEROXIDASE, NEUTRAL RED, SERPENTINE CORD, AND NIACIN TESTS WITH M. TUBERCULOSIS, ATYPICAL ACID-FAST BACILLI, AND SAPROPHYTIC MYCOBACTERIA

Strain	T-Test	P-Test	NR-Test	SC-Test	N-Test
Human Tubercle Bacilli					
A-23	−	+	+	+	+
A-24	−	+	+	+	+
A-25	−	+	+	+	+
A-26	−	+	+	+	+
A-27	−	+	+	+	+
A-28	−	+	+	+	+
A-29	−	+	+	+	+
A-30	−	+	+	+	+
A-31	−	+	+	+	+
A-32	−	+	+	+	+
A-33	−	+	+	+	+
A-34	−	+	+	+	+
A-35	−	+	+	+	+
A-36	−	+	+	+	+
A-37	−	+	+	+	+
A-38	−	+	+	+	+
A-39	−	+	+	+	+
A-40	−	+	+	+	+
A-41	−	+	+	+	+
A-42	−	+	+	+	+
A-43	−	+	+	+	+
A-44	−	+	+	+	+
CDC-1	−	+	+	+	+
CDC-2	−	+	+	+	+
CDC-3	−	+	+	+	+
H37Rv	−	+	+	+	+
Atypical Mycobacteria					
Photochromogens					
AP-9	34+	−	−	−	−
AP-10	29+	−	−	−	−
AP-11	29+	−	−	−	−
AP-12	29+	−	−	−	−
AP-13	27+	−	−	−	−
AP-14	24+	−	−	−	−
AP-15	16+	−	−	−	−
AP-16	12+	−	−	−	+
AP-17	−	−	−	−	−
AP-18	−	−	−	−	−
Scotochromogens					
AS-14	41+	−	−	−	−
AS-15	41+	−	−	−	−
AS-16	40+	−	−	−	−
AS-17	39+	−	−	−	−
AS-18	37+	−	−	−	−
AS-19	35+	−	−	−	−
AS-20	33+	−	−	−	+
AS-21	31+	−	−	−	−
AS-22	30+	−	−	−	−
AS-23	28+	−	−	−	−
AS-24	25+	−	−	−	−
AS-25	19+	−	−	−	−
AS-26	19+	−	−	−	−
AS-27	15+	−	−	−	+
AS-28	−	−	−	−	−
Saprophytic Mycobacteria					
M. smegmatis-a	1+P	−	−	−	−
M. smegmatis-b	1+P	−	−	−	−
M. smegmatis-c	1+P	−	−	−	−
M. smegmatis-d	1+P	−	−	−	−
M. phlei-a	1+P	−	−	+	+
M. phlei-b	1+P	−	−	+	+
M. butyricum	1+P	−	−	+	−

P=pellicle formation. Numbers=the day growth was first observed.

any of the tubercle bacilli, but did support the growth of 88 per cent of the atypical strains (8 photochromogens and 14 scotochromogens), and 100 per cent of the saprophytes. Growth of the atypical mycobacteria was slow and dysgonic, requiring from 12 to 34 days for initial development of the photochromogens, and from 15 to 41 days for the scotochromogens. The saprophytes grew rapidly and luxuriantly in one day with pellicle formation.

All the tubercle bacilli gave positive results with the peroxidase, neutral red, serpentine cord, and niacin tests, whereas all of the atypical and saphrophytic strains, with light exceptions, gave negative results with these tests. As observed previously,[3] slight to moderate degrees of cord formation were exhibited by three of the saprophytic organisms. However, their morphologic patterns were sufficiently characteristic to distinguish them from the type of cording found in the tubercle bacilli.

One of the photochromogens, two of the scotochromogens, and two of the saprophytic strains gave positive niacin tests, but the reactions were slight compared with the reactions of the tubercle bacilli which were either moderate or intense. In repeat niacin tests, in which one to four week old stock cultures of Proskauer-Beck and Löwenstein-Jensen media were used, all of the atypical and saprophytic mycobacteria gave either negative or doubtful reactions, while the tubercle bacilli, in most instances, exhibited lesser degrees of positivity compared with the results obtained with cultures from five to six weeks old. Two strains of tubercle bacilli gave negative niacin reactions with cultures one week old, doubtful to slightly positive results with cultures from two to four weeks old, and moderately to intensely positive reactions with cultures five weeks old. Because of these observations, it was decided to use cultures at least five weeks old before testing the strains for niacin content. That niacin concentration increases with the age of the culture has been pointed out previously by Gilani and Selkon,[10] and Konno.[11] Regardless of the methods employed, it has been observed that human type tubercle bacilli, in most instances, give more marked niacin reactions than other mycobacteria. Accordingly, the niacin test has proved helpful for distinguishing human strains of tubercle bacilli from other mycobacteria.

SUMMARY

From these results it can be seen that the peroxidase, neutral red, serpentine cord, and niacin tests are able, in most instances, to distinguish human tubercle bacilli from atypical and saprophytic mycobacteria, but they can not differentiate the atypical from the saprophytic group of organisms. On the other hand, the thioglycollate test is able, in most instances, to distinguish between all three groups, and when used in conjunction with the other tests, differentiation is further facilitated. All these tests are easy to perform, and have proved useful for group differentiation of *M. tuberculosis*, atypical acid-fast bacilli, and saprophytic mycobacteria.

RESUMEN

Según estos resultados puede verse que las reacciones de la peroxidasa, de la cuerda serpentina y de la niacina, son capaces de distinguir en la mayoría de los casos, el bacilo tuberculoso humano de las micobacterias atípicas y saprofitas, pero no pueden diferenciar las atípicas de las saprofitas. Por otra parte, la reacción del tioglicolato es capaz en la mayoría de los casos, de distinguir entre estos tres grupos y cuando se usa en combinación con las otras reacciones, la diferenciación es más fácil aún.

Todas estas reacciones son fáciles de realizar y se han demostrado útiles para la diferenciación del grupo de *M. tuberculosis*, bacilos atípicos ácido-resistentes y micobacterias saprofitas.

RESUMÉ

D'après les résultats rapportés par l'auteur, on peut voir que la peroxydase, le rouge neutre, la structure en cordon sinueux, et les tests à la niacine sont capables, dans la plupart des cas, de distinguer les bacilles tuberculeux ils ne peuvent différencier les microbes atypiques des germes saprophytés. D'un autre côte, le test au thioglycollate est capbale, dans la plupart des cas, de distinguer entre les trois groupes et lorsqu'il est utilisé en association avec les autres tests, la differenciation est alors facilitée. Tous ces tests sont faciles à pratiquer, et se sont montrés utiles pour différencier du groupe des M. tuberculosis les bacilles atypiques acido-résistants, et les mycobactéries saprophytes.

ZUSAMMENFASSUNG

Aus diesen Resultaten läßt sich ersehen, daß die Proben mit Peroxidase, Neutral-rot, Schlängelung und Nikotinsäure in den meisten Fällen imstande sind, Tuberkelbazillen vom humanen Typ zu unterscheiden von atypischen und saprophytischen Mycobakterien; sie ermöglichen aber keine Differenzierung zwischen den atypischen und den saprophytischen Gruppen dieser Organismen. Anderersits ist dr Thioglygollat-Test in den meisten Fällen imstande, zu unterscheiden zwischen allen drei Gruppen. Wird er in Verbindung mit den anderen Proben eingesstzt, ist die Differenzierung noch weiter erleichtert. Alle diese Proben sind leicht durchzuführen und haben sich als nützlich erwiesen zur Gruppen-Differenzierung von *M. tuberkulosis*, atypischen säurefesten Bazillen und saprophytischen Mycobakterien.

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Five-Year Survival After Surgery for Bronchogenic Carcinoma

An Analysis of Twenty-one Cases

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Introduction

Since the prognosis of bronchogenic carcinoma is so poor,[1-9] the data for 21 patients who survived five years or longer after surgery for this disease were examined in the hope of discovering factors influencing long-term survival. The results of this study are the basis of this report.

Clinical Material

During the five years beginning January 1, 1949, and ending December 31, 1953, the diagnosis of bronchogenic carcinoma was established in 347 patients at the Cleveland Clinic (Table 1). Of these, 209 (60 per cent) underwent thoracotomy, and 138 (40 per cent) were considered to have inoperable far-advanced disease. Of the 209 patients operated upon, lesions in 124 were not resectable (59 per cent of the patients explored), and in 85 were resectable (41 per cent of the patients explored). The longest known survival in the nonresectable group was a patient who lived two years and four months after thoracotomy. Of the 85 in whom resections could be carried out, 21 lived five years or longer after operation. The records of the survivors were examined as to age, sex, symptoms, signs, roentgen, bronchoscopic, and pathologic findings, and surgical procedures performed.

Clinical Data

The patients ranged in age from 38 to 76 years; most of the group were between 45 and 65 years. Men outnumbered women nine to one. The range of age and ratio of sexes of these patients conform to those generally reported, and suggest that these factors do not distinguish these patients from those who do not survive.

There were six asymptomatic patients among the 21 long-term survivors. The percentage of asymptomatic patients in this group is much higher than that in the entire group operated upon; however, symptoms when present are the same and the duration of symptoms is, if anything, longer. The commonest symptoms were cough, hemoptysis, and loss in weight, and they were present for an average of 10 months.

The physical findings were normal in seven patients, five of whom were asymptomatic; the other two had coughs and hemoptysis. In four others the results of examination of the chest were normal, and the only abnormal physical findings were clubbing of the fingers and toes, and swelling of the ankles and feet. In the other 10 dullness, diminished breath sounds and rales were noted in the region of pulmonary involve-

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ment. Only one half of the patients with curable lung cancer had abnormal physical findings demonstrated on examination of the chest. It is noteworthy that 38 per cent of the inoperable patients had no abnormal physical findings reported after examination of the chest.

The chest roentgenogram was much more reliable than physical examination. The roentgenogram was abnormal in virtually all cases. The lesions were well circumscribed and peripheral in six patients, all of whom had been asymptomatic. In the others, hilar shadows with atelectasis and infiltrates extending out into the lung fields were noted. Although the radiographic findings varied from case to case, the extent of atelectasis never exceeded one lobe. Pleural effusion, diaphragmatic paralysis, and bone metastasis were absent.

Bronchoscopy was performed in 16 of the 21 long-term survivors. Of the five not examined endoscopically, four had peripheral lesions. For seven the bronchoscopic findings were normal, but for one of them, a smear of bronchial secretions demonstrated malignant cells. For nine the findings were described as abnormal, in six of whom the tumors were seen and were successfully biopsied. In the other three patients the abnormalities noted respectively, were: extrinsic pressure on a bronchus, bleeding from a bronchus, and friability of the mucous membrane. In the last-mentioned patient a biopsy showed carcinoma, and smears showed malignant cells. Positive proof of the diagnosis was obtained from one half of the endoscopies in this group of patients.

Surgery

All of the long-term survivors were operated upon and, with the exception of one patient with recurrent carcinoma, none have received roentgen therapy. Lobectomy was performed in nine patients, and pneumonectomy in 12. In six who underwent lobectomy it was the opinion of the operating surgeon (D. B. E.) that because of the peripheral location of the tumor, the procedure offered as much chance for cure as did pneumonectomy. In two lobectomy was performed because each patient presented serious limitation of pulmonary function. In one patient palliative lobectomy was done because the tumor adhered to the aortic arch. Pneumonectomy was carried out in 12, in two of whom it was regarded as palliative.

Pathology

The histologic classification of bronchogenic carcinoma used here distinguishes four categories: (1) squamous-cell carcinoma, (2) adenocar-

TABLE 1 — DATA OF 347 PATIENTS WITH PROVED BRONCHOGENIC CARCINOMA SEEN AT THE CLEVELAND CLINIC BETWEEN JANUARY 1, 1949, AND DECEMBER 31, 1953

Subject	Number of Patients	Percentage
Total proved cases	347	100
Exploratory thoracotomy	209	60
Resection	85	25 (41 per cent of those explored)
Five-year survival	21	6 (25 per cent of those resected)

cinoma, (3) undifferentiated carcinoma, and (4) small-cell carcinoma. Of the 21 five-year survivors, 12 had squamous-cell carcinoma, five adenocarcinoma, three undifferentiated carcinoma, and one small-cell carcinoma (Table 2). The predominance of squamous-cell carcinoma and the paucity of the undifferentiated tumors is significant and consistent with the reputations of these cancers. Cell type has a definite bearing upon survival of the patient. Squamous-cell carcinoma offers the best prognosis. The five-year survival of a patient having small-cell carcinoma is almost in the category of a surgical curiosity.

Lymph-node metastasis was present in seven of the 21 long-term survivors. All had undergone pneumonectomy. In five of the seven the carcinoma was squamous-cell, in one adenocarcinoma, and in one undifferentiated carcinoma. In four only one involved lymph node was found in each, while in the other three patients there were three, five, and five positive nodes, respectively. It is significant that the percentage of lymph-node metastasis is as high as it is. In fact, two of these patients are alive almost 10 years after operation. The presence of lymph-node metastasis is doubtless a bad prognostic sign, but it does not render survival impossible, particularly if the carcinoma is of the squamous-cell type.

Neoplastic invasion of the pulmonary vessels was found in two patients; the two specimens were removed at lobectomy. Neither patient had lymph-node metastasis and both are still living. The recent studies of this facet of the pathologic picture indicate that vascular invasion is an ominous finding, particularly if the lymph nodes are involved too. Again, the fact that patients survive long after surgery, even with vascular invasion, is perplexing.

Results of Surgery

Nine lobectomies and 12 pneumonectomies were performed in the long-term survivors. In the resectable group as a whole there were 29 lobectomies and 56 pneumonectomies. The five-year survival rate is 31 per cent for those who underwent lobectomy and 16 per cent for those who underwent pneumonectomy; 25 per cent for the resected group as a whole. There was an operative mortality of 12 patients; three died after lobectomy and nine after pneumonectomy. There are two late recurrences of carcinoma. If the survival rate is corrected for recurrences and postoperative deaths, then 19 of 73 patients or 26 per cent are living and well and free of disease five years or longer after operation.

TABLE 2 — DATA FOR 21 PATIENTS SURVIVING FIVE YEARS OR LONGER AFTER SURGERY FOR BRONCHOGENIC CARCINOMA

Histologic type of carcinoma	Number of Patients who Underwent Lobectomy	Pneumonectomy
Squamous-cell carcinoma	4	8*
Adenocarcinoma	3	2**
Undifferentiated carcinoma	2	1**
Small-cell carcinoma	0	1
Total	9	12

*Five had lymph-node metastasis.
**One had lymph-node metastasis.

Of the 73 who survived operation, 40 died before the second postoperative year ended; and 12 died between the beginning of the second and the end of the fourth postoperative years. Twenty-one lived five years or longer.

The longest survivors all had squamous-cell carcinoma. Four are alive almost 10 years after operation, two of whom had lymph-node metastasis.

Discussion

It is at once apparent that the pattern of survival is complex. Symptoms and signs are late manifestations of lung cancer. It would be better to make the diagnosis before symptoms appear, and to do this, chest roentgenograms must be taken on a survey basis. As experience accumulates with the treatment of lung cancer discovered in this manner, it is at once evident that the resectability rate is much higher than in the symptomatic cases. In fact, it approaches 100 per cent.[10-12] Whether the cure rates also will prove to be higher remains to be seen. Certainly more patients will be given the opportunity to survive than heretofore.

It is perhaps of some significance that the cancers in six of our 21 five-year survivors were discovered while the patients were still asymptomatic. In a seventh, the cancer was discovered while the patient still was asymptomatic, but deterioration to a less favorable stage of the disease occurred during the succeeding 18 months. This, incidentally, is one of the patients with recurrent carcinoma. So, while earlier diagnosis offers hope for more long-term survivors, it is by no means a guarantee of cure.

With respect to therapy, acceptance of the need for exploratory thoracotomy for diagnosis as well as treatment is becoming increasingly widespread. This is particularly necessary in the survey cases where bronchoscopic findings so often are normal.

So far as the surgical procedure itself is concerned, there have been two trends away from the standard pneumonectomy: (1) toward radical pneumonectomy[13,14] and, (2) toward the more liberal use of lobectomy[12,15] particularly in early cases. The experience with operative treatment in our hospital includes patients treated by lobectomy and by standard pneumonectomy. There were no so-called "radical pneumonectomies" performed incorporating extensive mediastinal dissections. When, in this series of patients, the extent of the operation is related to survival, it is seen that 31 per cent of the patients who underwent lobectomy lived five years, but only 16 per cent of those who underwent pneumonectomy lived five years. Although lobectomy may seem to be superior to pneumonectomy, actually, the comparison reflects the fact that lobectomy was done for more favorable cancers.

The histologic type of the tumor is a factor in survival. Squamous-cell cancer appeared to be more favorable than the other types, and yet four patients with undifferentiated carcinoma, one of which was a small-cell tumor survived five years or longer. Lymph-node metastasis (particularly in cases of squamous-cell carcinoma) did not preclude survival, nor did vascular invasion, which was found in two patients, although in none were both present in the same patient. Such factors as genetic susceptibility, host resistance and immunity, and the inherent growth potential of the tumor are poorly understood, if at all, and yet must certainly play decisive roles.

It would appear that an asymptomatic peripheral squamous-cell carcinoma without lymph-node metastasis, vascular invasion, or distant spread has the most favorable prognosis. This lesion will have to be detected on a survey chest roentgenogram. The physical and bronchoscopic findings will in all probability be completely normal. The lesion may grow slowly for years,[16] but must be removed when it is discovered. It is likely to be cured by lobectomy as well as by pneumonectomy. However, not all such lesions will be cured, and patients with less favorable lesions will survive for reasons that at present are obscure. It may well be that until chemotherapeutic agents are developed that can inhibit or destroy malignant cells, or the cause of lung cancer is discovered, there will be little change in the cure rate from the use of present methods of detection and treatment.

SUMMARY

1. The diagnosis of bronchogenic carcinoma was established in 347 patients at the Cleveland Clinic between January 1, 1949, and December 31, 1953.

2. Exploratory thoracotomy was carried out in 209 patients but in only 85 was pulmonary resection feasible. Of the latter, 21 patients lived five years or more after surgery.

3. The records of the survivors were scrutinized from the standpoint of age, sex, symptoms, signs, roentgen, bronchoscopic and pathologic findings, and surgical procedure performed.

4. No feature consistently distinguished the survivors from the nonsurvivors, although lack of symptoms, peripheral location of the tumor, and squamous-cell type of cancer were frequent findings in the survivors.

5. Thirty-one per cent of the patients who underwent lobectomy lived five years, but only 16 per cent of those who underwent pneumonectomy lived that long. This reflects the fact that lobectomy was done for more favorable cancers rather than that lobectomy is a procedure superior to pneumonectomy.

6. Factors other than those studied, e. g., host resistance and immunity, and inherent growth potential of the tumor must also influence survival, and the role of these is at present obscure.

RESUMEN

1. En 347 enfermos que acudieron a la Clínica de Cleveland entre Enero 1, de 1949 y Diciembre 31 de 1953, se llegó al diagnóstico de carcinoma bronquiogénico.

2. Se llevó a cabo la toracotomía exploradora en 209, pero sólo en 85 se pudo hacer la resección. De estos últimos, 21 enfermos vivieron 5 o mas años después de operados.

3. Los expedientes de los sobrevivientes se examinaron desde el punto de vista de edad, sexo, síntomas, radiología, signos, hallazgos broncoscópicos y patológicos y el procedimiento quirúrgico empleado.

4. Ninguna característica distinguió a los sobrevivientes de los que no lograron serlo aunque la falta de síntomas, la ubicación periférica del tumor, y el tipo escamocelular del cáncer fueron hallados frecuentemente en los que sobrevivieron.

5. Treinta y uno por ciento de los enfermos a quienes se hizo lobectomía, vivieron cinco años pere sólo 16 por ciento de los que sufrieron neumonectomía vivieron ese lapso. Esto refleja el hecho de que la lobectomía se realizó en los cánceres mas favorables mas bien que significar que la lobectomía sea superior a la neumonectomía.

6. Otros factores ademas estudiados tales como resistencia del huésped e inmunidad y el inherente potencial de crecimiento del tumor deben influir también en la sobrevida y el papel de estos factores es actualmente obscuro.

RESUMÉ

1. Le diagnostic de cancer bronchique fut établi chez 347 malades à la Clinique Cleveland entre le Ier janvier 1949 et le 31 décembre 1953.

2. Une thoracotomie exploratric fut pratiquée cnez 209 malades, mais une résection pulmonaire fut räalisable chez 85 malades seuelment. Parmi ceux-ci 21 vécurent cinq ans et plus après la chirurgie.

3. Les listes des survivants furent examinées au point de vue de l'âge, du sexe, des symptômes, des signes, de la radiologie, des constatations bronchoscopiques et anatomo-pathologiques, et en fonction du procédé chirurgical utilisé.

4. Aucun trait ne distingue d'une façon significative les survivants des non-survivants, bien qu'un manque de symptômes, une localisation périphérique de la tumeur, et un type de cancer à cellules épidermoides fussent des constatations fréquentes chez les survivants.

5. 31% des malades qui subirent une lobectomie survécurent cinq ans, mais 16% seulement de ceux qui subirent une pneumonectomie survécurent aussi longtemps. Ceci reflète le fait que la lobectomie fut faite pour des cancers à prorostic plus favorable plutôt que parce que la lobectomie est un procédé supérieur à la pneumonectomie.

6. Des facteurs autres que ceux qui ont été étudiés, c'est-à-dire la résistance de l'individu et l'immunité, et le potentiel de croissance de la tumeur doivent aussi influencer la survie, le rôle de ces facteurs est jusqu'à présent mystérieux.

ZUSAMMENFASSUNG

1. Die Diagnose eines bronchogenen Carzinoms wurde zwischen dem 1. 1. 1949 und dem 31. 12. 1953 in der Cleveland-Klinik bei 347 Patienten gestellt.

2. Die diagnostische Thorakotomie wurde bei 209 Patienten ausgeführt, jedoch war eine Lungenresektion nur in 85 Fällen möglich. Von dieser Gruppe lebten 21 Kranke 5 Jahre oder länger nach dem Eingriff.

3. Die Krankengeschichten der Überlebenden wurden überprüft nach den Gesichtspunkten von Alter, Geschlecht, subjektiven und objektiven Krankheitszeichen, röntgenologischen, bronchoskopischen und pathologisch-histologischen Befunden, sowie dem operativen Vorgehen.

4. Nicht ein einziges regelmässig vorliegendes Merkmal unterschied die Überlebenden von den icht Überlebenden, wenngleich das Fehlen von Symptomen, eine periphere Tumorlokalisation und der Plattenepithel-Zelltyp des Krebses unter den Überlebenden häufiger gefunden wurde.

5. 31% der Kranken, bei denen eine Lobektomie vorgenommen worden war, überlebten 5 Jahre; aber nur 16% von denjenigen, bei denen eine Pneumonektomie vorgenommen worden war, lebten gleich lang. Darin kommt eher die Tatsache zum Ausdruck, daß die Lobektomie bei günstigeren Carzinomfällen erfolgte, als daß die Lobektomie eine Methode ist, die der Pneumonektomie überlegen ist.

6. Andere Faktoren—als die oben untersuchten, d.h. Widerstand des Körpers und Immunität, und das dem Tumor innewohnende Wachstumspotential-müβ en natürlich auch die Überlebenszeit beeinflussen; jedoch ist deren Rolle im Augenblick noch ninklar.

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SECTION ON CARDIOVASCULAR DISEASES

Effect of Transthoracic Endoscopic Sympathectomy on the Cardiac Neurovegetative Equilibrium and on Angina Pectoris*, **

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Since the first attempts of T. Jonnesco[1] to treat angina pectoris by means of cervico-thoracic sympathectomy, many surgeons have applied similar techniques with satisfactory results in the majority of instances.[2] Nearly without exception, the operations were performed with the declared purpose to sever sensory, pain-conveying, afferent nervous pathways, and without realization of the fact that (except in the case of exclusive section of the posterior roots), the norepinephrine-discharging, pain-producing efferent sympathetic fibers[3] were, likewise, interrupted.

In animal experiments, it has been shown that electrical stimulation of the cardiac sympathetic nerves is followed by an accumulation of catecholamines,[4,5] especially of norepinephrine,[6] in the myocardium, whereas the cardiac catecholamine stores are largely depleted by sympathectomy.[7-9]

In view of these experimental findings, it appeared of interest to study the effect of sympathetic denervation on the function of the normal human heart by means of the "chronodynogram," i.e. graphic measurement of the lengths of the isometric and isotonic contraction periods of the left ventricle (method of Blumberger).[10] Using the second standard lead of the electrocardiogram, the phonocardiogram over the upper sternum, and registration of the carotid pulse wave on the neck by means of a multi-channel apparatus, the length of the total systole of the left ventricle (Q or beginning of R wave to first vibration of second heart sound) is measured and expressed in thousandths of a second (paper speed 10 cm. per second). From this dimension, the length of the isotonic or ejection period (point of steep ascent of the carotid pulse wave to bottom of its incisura) is subtracted. The difference indicates the length of the isometric period.

The isotonic period is of no particular significance, as far as the problem of neurovegetative effects on the heart muscle is concerned, but the isometric or tension period (TP) is characteristically shortened by adrenergic and lengthened by cholinergic influences.[11] Accordingly, this

*This study was aided by grants from the U. S. Public Health Service, National Heart Institute (H-2169[C]), the Vermont Heart Association, the Fulbright Commission, U. S. Department of State (Vienna), and the Universitätsbund Innsbruck.

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parameter has proved useful for evaluation of the adrenergic-cholinergic equilibrium in cardiac dynamics.[11,12]

Persons without cardiac pathology were available for this study, in that the endoscopic transthoracic sympathectomy, as practiced by one of us (K.) since 1940,[13,14] is indicated in a variety of non-cardiac conditions, such as vascular neuroses of the upper extremities, acrocyanosis, hyperhidrosis, neuralgias, etc.[14] In addition, two patients with angina pectoris were included in our present series.

Methods

In all test subjects, the chronodynograms, heart rate and blood pressure were recorded before and at varying time intervals after sympathectomy, with a 6-channel Multiskriptor apparatus (Hellige, Freiburg i.Br.), as described elsewhere.[11] The tracings were made while the test subjects were resting in recumbent position two hours or more after light meals. Each test was repeated after 15 or more minutes, in some instances also on the following day. Each reading represents the average of 20 to 60

TABLE 1

Pat. No.	Sex	Age (yrs.)	Bl. pr. (mm Hg)	No. of days between operation and tests		Isometric (TP) period (1/1000 sec.)		Heart rate per min.		Pulse pressure (mm Hg)		Remarks
				Left	Right	Ave. before op.	per cent deviat. after op.	Ave. before op.	per cent deviat. after op	Ave. before op.	per cent deviat. after op.	
1	female	37	123/ 68	2	253	66	+50	91	−23	55	−22	Non-card.
				77	328		+42		−22		−22	
2	male	44	151/ 98	132	—	93	+33	63	− 8	53	−26	Non-card.
				189	5		+32		+ 3		−28	
3	female	27	115/ 54	—	3	95	+23	64	+ 6	61	−20	Non-card.
					27		+28		− 8		−20	
4	female	25	109/ 79	—	13	95	+21	59	− 7	30	+20	Non-card.
				3	19		+ 6		+ 9		+33	
5	male	34	143/ 73	7	—	83	+20	75	− 3	70	− 7	Non-card.
6	male	55	83/ 60	—	2	79	+17	76	+11	23	− 4	Non-card.
7	male	43	115/ 62	4	—	85	+15	80	−13	53	−23	Non-card.
8	male	60	121/ 65	7	—	99	+13	55	+ 9	56	−45	Non-card.
9	female	59	117/ 70	6	—	115	+ 8	66	− 9	47	± 0	Non-card.
10	female	21	111/ 78	16	4	115	+ 5	55	−16	33	+24	Non-card.
				62	50		+ 7		−29		+43	
11	male	38	118/ 77	5	—	97	± 0	82	−16	41	+12	Non-card.
				52	45		+ 5		+ 7		+29	
12	female	18	118/ 68	54	—	111	− 3	78	−21	50	+ 2	Non-card.
				56	1		−22		− 1		−20	
13	male	18	158/ 70	—	2	95	− 4	63	−14	88	−15	Non-card.
14	male	18	140/ 60	3	1	95	− 8	80	− 3	80	+11	Non-card.
15	male	57	116/ 77	69	—	111	−19	61	+ 5	39	± 0	Non-card.
16	female	22	113/ 73	2	2	78	−14	83	+ 4	40	+25	Non-card.
				8	8		−30		− 5		+33	
				58	58		−30		− 8		− 3	
				171	171		− 8		+ 4		+18	
17	male	54	127/ 61	75	—	73	+49	75	− 3	66	−18	Ang. pect.
				372			+31		− 1		−15	
18	male	46	148/106	4	—	118	+10	70	− 8	42	+14	Ang. pect.
				322			+ 3		− 9		+60	

individual heart beat measurements, obtained from two to four test tracings. At the time of the tests, no medication with cardiovascular action was administered.

The transthoracic endoscopic sympathectomy was carried out under local anesthesia either unilaterally (right or left) or bilaterally, in one or two sessions. In six instances, the operation was combined with transthoracic unilateral or bilateral splanchnicotomy. In one case, right-sided vagotomy had preceded the bilateral sympathectomy.

Results

(a) Non-cardiac patients.

The findings obtained in 16 non-cardiac patients concerning the length of the isometric or tension period (TP), heart rate and pulse pressure are represented in Table 1.

In response to transthoracic sympathectomy, all three parameters varied from person to person in wide ranges in both directions. However, when the tests were repeated in the same patients at different time intervals after the operation (with or without a second contralateral sympathectomy inbetween), their qualitative pattern of response (either upward or downward) remained the same in nearly all instances, as far as the TP and pulse pressure were concerned. The responses of the heart rate, on the other hand, were less striking percentage-wise and varied in quite an irregular fashion in identical individuals.

No significant relationship existed between the magnitude of the preoperative average values and the type (positive or negative) or degree

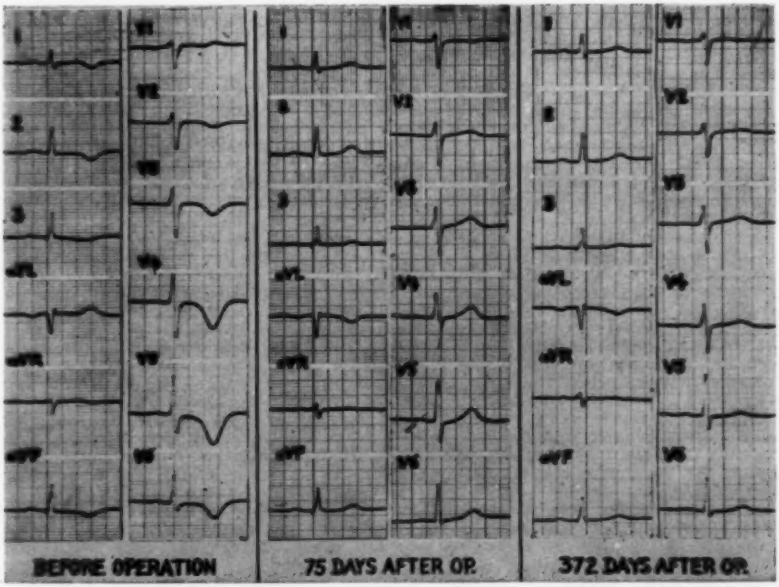

FIGURE 1: Electrocardiograms of patient 17 before and after left-sided transthoracic endoscopic sympathectomy (+left-sided splanchnicotomy). Marked clinical improvement of angina pectoris.

of the postoperative deviations in either one of the three recorded parameters.

Blood pressure changes were insignificant, except for a reduction in case 2 from 151/98 to 124/86.

Where transthoracic splanchnicotomy was carried out (cases 10, 15 and 17: left side; case 11: right side; cases 4 and 16: bilateral), it did not seem to affect the cardiac condition significantly, nor did earlier preceding right-sided vagotomy (case 1) prevent the development of the majority pattern of response after sympathectomy.

(b) Patients with angina pectoris.

At the bottom of Table 1, two patients with severe angina pectoris are represented. Both were sympathectomized only on the left side, and in both a prolongation of TP appeared (marked in patient 17 who had had a short TP before surgery, and slight in patient 18), accompanied by a slight reduction of the heart rate. The blood pressure was not altered. The pulse pressure fell in patient 17 and rose in patient 18.

Patient 17 became symptom-free immediately after the operation, for one month. During the following 10 months, some mild symptoms recurred from time to time, but altogether his condition remained greatly improved. The originally pathological electrocardiogram of this patient was found normalized on two occasions (75 and 372 days) after sympathectomy (Fig. 1).

In case 18, improvement set in only a few weeks after the operation, but the symptoms disappeared completely and did not return during the following 10 months. The electrocardiogram had been uncharacteristic from the beginning.

Discussion

The prolongation of the isometric (tension) period (TP) of the left ventricle which occurred in the majority (72 per cent) of all cases after unilateral or bilateral transthoracic sympathectomy (without or with unilateral or bilateral transthoracic splanchnicotomy) indicates a diminution of inotropic cardiac action. It can be assumed to correspond to the cholinergic (vagal) preponderance which results from a partial or complete sympathetic denervation of the heart. Reduction of the pulse pressure occurred in 56 per cent of the cases, probably due to the same mechanism. The behavior of the heart rate was too irregular to permit any conclusions. Apparently, the inotropic mechanisms of the heart are more sensitive to sympathetic denervation than the chronotropic ones.

The seemingly paradoxical shortening of TP which was persistently maintained, e.g., in the case of patient 16 over a period of more than five months, is possibly to be explained as a manifestation of Cannon's "law of denervation" according to which the catecholamine sensitivity of sympathetically denervated structures is greatly augmented, and which has more recently been confirmed also in instances of functional sympathetic "denervation" (catecholamine deprivation of cardiovascular tissues) through ganglionic blockade[15] or rauwolfia drugs.[16] This would mean in the present cases that their partly or wholly sympathectomized hearts had become oversensitive to whatever active catecholamines (norepinephrine, epinephrine) may have reached them either from remaining sympathetic fibres or through the blood stream. Individual differences in relative reactivity to two mutually antagonistic factors ([a] absolute loss of catecholamines, and [b] exaggerated catecholamine sensitivity, caused by [a]); combined with the individual magnitude of absolute cardiac cholinergic activity, may account for the prevalence of either negative or positive inotropic cardiac reactions to sympathectomy.

The marked and prolonged subjective and partly also objective (EKG) improvement in two cases of angina pectoris is in agreement with previously published observations of the one of us (K) on 52 angina patients, operated with the same technique.[14] Similar favorable and lasting results had been obtained in many instances of angina pectoris by other workers with other methods of cardiac sympathetic denervation, involving major surgical procedures and their inherent hazards.[2]

There can be little doubt that the functional mechanism responsible for the clinical improvements after cardiac sympathectomy consists essentially of a reduction or

abolition of the influx of hypoxiating, angina-producing norepinephrine from postganglionic cardiac sympathetic fibres supplying the heart muscle. (In contrast to the reflectory vagus-stimulating effect of injected circulating norepinephrine which acts primarily on the peripheral pressoreceptors, norepinephrine discharged within the myocardium exerts purely adrenergic effects on the heart.)

SUMMARY

In the majority of 16 non-cardiac and in two angina pectoris patients, unilateral or bilateral endoscopic transthoracic sympathectomy (method of Kux) was followed by signs of augmented cholinergic preponderance in cardiac dynamics (especially prolongation of the isometric period of the left ventricle).

An opposite type of reaction in a minority of instances is tentatively explained on the basis of Cannon's "law of denervation" (=oversensitivity of sympathetically denervated structures to remaining catecholamines, e.g. circulating epinephrine).

Marked clinical improvement in two cases of angina pectoris (like that after other types of cardiac sympathetic denervation) is attributed to a reduction of angina-producing norepinephrine discharges into the poorly vascularized myocardium of individuals with coronary atherosclerosis.

RESUMEN

En la mayoría de 16 no cardicos y en dos con angina de pecho, se hizo simpatectomía transtorácica unilateral o bilateral por vía endoscópica (Método de Kux) a lo que siguieron signos de un aumento de preponderancia colinérgica en la dinámica cardiaca (especialmente prolongación del período isométrico del ventrícula izquierdo).

Un tipo opuesto de reacción en la minoría de casos se intenta explicar basándose de la "ley de denervación" de Cannon (Supersensibilidad de las estructuras con denervación simpática a las catecolaminas restantes, y a la epinefrina circulante).

La marcada mejoría clínica en dos casos de angina pecho (como después de otras formas de denervación simpática) se atribuye a una reducción de la descarga de norepinefrina que es causante de angina, dentro del miocardio pobremente vascularizado de los individuos con ateroesclerosis coronaria.

RESUMÉ

Chez 16 malades non-cardiaques et chez deux atteints d'angine de poitrine, une sympathectomie transthoracique endoscopique unilatérale ou bilatérale (méthode de Kux) fut suivie dans la majorité des cas de signes d'augmentation de la prépondérance cholinergique dans la dynamique cardiaque (particulièrement prolongation de la période isométrique du ventricule gauche).

L'auteur tente d'expliquer le type contraire de réaction constaté dans une minorité de cas en faisant état de la "loi d'énervation" de Cannon (=hypersensibilité des structures énervées par le sympathique aux cathécolamines restants, c'est-à-dire à l'épinéphrine circulante).

Une amélioration clinique nette dans deux cas d'angine de poitrine (comme celle constatée après d'autres types d'énervation sympathique cardiaque) est attribuée à une réduction de la décharge de norepinéphrine produisant l'angine de poitrine dans le myocarde pauvrement vascularisé d'individus atteints d'athérosclérose coronarienne.

ZUSAMMENFASSUNG

Bei der Mehrzahl der 16 Nicht-Herzkranken und bei 2 Patienten mit Angina pectoris folgten auf die ein- oder beidseitige endoskopische transthorakale Sympathektomie (nach der Methode von Kux) Zeichen eines erhöhten cholinergischen Überwiegens in der Herzdynamik (besonders eine Verlängerung der isometrischen Periode der linken Kammer).

Ein entgegengesetzter Reaktionstyp, wie er in einer Minderheit von Fällen auftritt, läßt sich etwa erklären auf der Basis von Cannon's "Gesetz der Denervation" (=Überempfindlichkeit der ihres Sympathikus beraubten Strukturen gegenüber verbleibenden Katecholaminen, d.h. zirkulierendem Epinephrin).

Die deutliche klinische Besserung bei 2 Fällen von Angina pectoris (ähnlich jener nach anderen Methoden cardialer Sympathikusdenervation) wird einer Reduzierung der die Angina bewirkenden Norepinephrine-Ausscheidung in einem schlecht durchbluteten Myocard bei Personen mit Arteriosklerose der Coronargefäße zugeschrieben.

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Left Atrial Myxoma: Surgical Cure

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It is indeed fortunate that the intracardiac myxoma which can be so disabling and often fatal has become a curable lesion within the last five years. The initial successful removal of an inter-atrial myxoma is credited to Crafoord[1] of Stockholm in 1954, and since then 13 additional cases have been reported.[2] This success is due chiefly to the development of diagnostic aids and the rapid expansion in the field of cardiac surgery. In 1945, Mahaim[3] had suggested angiocardiography as an aid in the diagnosis of cardiac tumors, and in 1953, Steinberg[4] reported three patients in whom cardiac tumors had been thus diagnosed. Since then, angiocardiography has been increasingly used in their detection.

Comprehensive reviews of cardiac tumors have been presented by Yater,[5] Prichard,[6] and Kaufman,[7] and including the year 1957, about 500 primary tumors of the heart had been reported. Their rarity, however, is noted by the fact that in a study of 480,331 autopsy cases by Strauss and Merliss, there were only eight cases or an incidence of but 0.0017 per cent.[8] The majority of patients are between 30 and 60 years of age with a wide range of three months to 68 years. While Prichard states sex distribution is about equal, McAllen[9] reports that the ratio between females and males is three to one. Myxomas are for the most part found in the atrial chambers of the heart with a threefold preponderance on the left.

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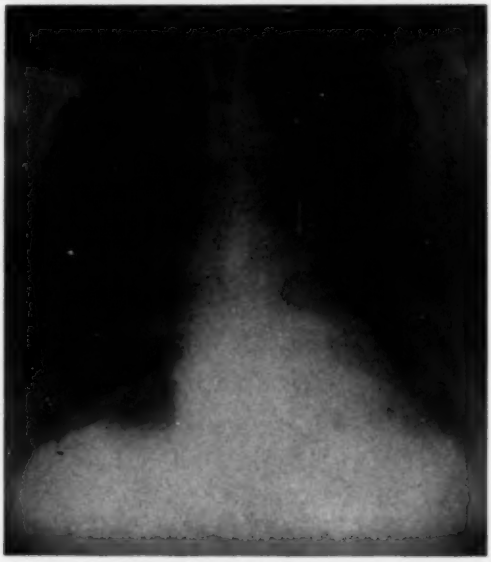


FIGURE 1: Pre-operative chest film, 1957, showing increased transverse heart diameter, enlarged left atrium, and prominent pulmonary outflow tract.

The following is a case report of a successful surgical removal of a myxoma from the left atrium of a 46 year old woman, in 1957, four years following the removal of a tumor embolus from the left common iliac artery.

Case Report

A 46 year-old white housewife was admitted to the hospital on January 7, 1957, for mitral commissurotomy. She had had progressive dyspnea for the preceding year, but no orthopnea, or hemoptysis. The patient gave no definite history of rheumatic fever, but in childhood was subject to joint pains. In 1953, at another hospital, she stated that a "blood clot" had been removed from a blood vessel in her left leg. One year ago, she had a stroke causing left hemiplegia, but recovered rapidly without sequellae. Her doctor's examination revealed mitral stenosis and auricular fibrillation.

On examination, she appeared healthy and younger than the stated age. The lungs were entirely clear and there was no fullness of the neck veins. The liver was not palpable and there was no ankle edema. The left heart border was percussed at the anterior axillary line, in the fifth interspace, the heart rate was 95/min. and the rhythm regular. There was a low-pitched systolic rumbling murmur best heard at the apex and along the left sternal border, ending with a high pitched presystolic component. The mitral first sound was loud with an opening snap and there was no thrill. The blood pressure was 105/80 mm. Hg. There was a left lateral abdominal incisional scar.

The chest roentgenogram showed the heart increased in diameter with slight enlargement of the left auricle. The pulmonary outflow tract appeared somewhat prominent (Fig. 1). The electrocardiogram suggested combined ventricular hypertrophy and routine laboratory studies were normal.

The pre-operative diagnosis was mitral stenosis and insufficiency. There was little doubt, by all concerned, that this was the most likely diagnosis, in spite of the absence of a rheumatic history.

On January 9, 1957, left thoracotomy was done with exploration of the left auricular area. A finger inserted into the left atrial chamber immediately passed through a widely patent and seemingly normal mitral valve orifice. During this time, a soft, mobile mass brushed the dorsum of the examining finger. The first impression was that the mass represented a clot, and the finger was rapidly withdrawn as the previously placed purse string suture was tied. Further discussion at the operating table emphasized the unlikelihood of an intra-atrial clot in the presence of a normal valve. It was at this time that the surgeon first considered the likelihood of a cardiac tumor. The visiting staff physician then recalled that the peripheral embolus removed from this patient in 1958 at another hospital was felt to be a tumor embolus by the hospital pathologist. Little significance appeared to have been attached to this finding at that

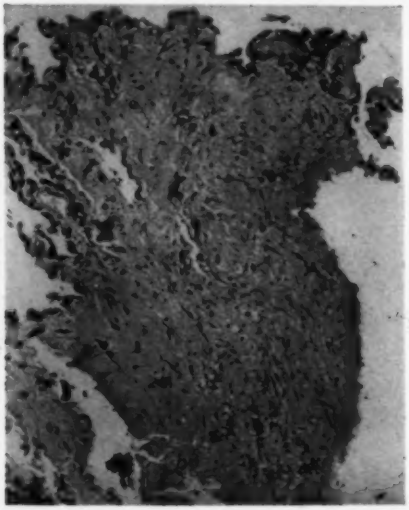


FIGURE 2: Embolic material surgically removed from the left common iliac artery, March 4, 1953. The material is composed of loose myxomatous stroma with numerous multinucleated giant cells and suggestion of encapsulation over polypoid processes. There is a thick-walled blood vessel on the left. (Hematoxylin and eosin, x 120).

time. Neither the patient's operative condition, nor the anesthetic status would allow re-exploration and excision of the tumor. The chest was closed.

During the patient's stay in the hospital, the slides of the tumor embolus were obtained and reviewed and the diagnosis confirmed by several other pathologists (Fig. 2).

Following the exploratory thoracotomy, the patient was discharged after a slow convalescence of five weeks. This period was characterized by elevated temperature and marked fatigue. On discharge, it was hoped that her condition would improve sufficiently to make re-operation possible.

On May 24, 1957, approximately five months following the original left thoracotomy, she was re-admitted for surgery. During the interim, she had shown gradual improvement in health, but had never been able to undertake routine activities because of easy fatigue and dyspnea. On examination, the left cardiac border was percussed, as before, at the left anterior axillary line. No murmur was audible and no thrill was felt. The second pulmonic sound was louder than the second aortic sound. There was a normal sinus rhythm.

The chest roentgenogram showed slight left ventricular enlargement with other chambers of the heart appearing normal. The electrocardiogram had not changed in pattern since the last entry.

The second thoracic operation was performed on May 27, 1957, under 30° centigrade hypothermia. After isolation of the inflow and outflow cardiac vessels, the tumor of

TABLE 1 — MYXOMA OF THE ATRIUM WITH SUCCESSFUL REMOVAL

Cases Published	Year	Age (Yr) and Sex	Site of Features	Accessory Operative Aids	Remarks
Crafoord	1955	40-50 F	Left	Extracorp. Circulation	Diagnosed by angiocardiography. Well one year later.
Bigelow co-authors	1955	56 F	Left 8 x 4 cm.	Hypothermia	Surgery for mitral stenosis. Well three months later.
Scannell co-authors	1956	33 F	Left 8½ x 3½ cm.	Hypothermia	Surgery for mitral stenosis. Well five months later.
Rahnson co-authors	1957	57 F	Left 4 x 5 x 6 cm.	Extracorp. Circulation	Surgery for mitral stenosis. Well six months later.
Hanlon	1957	61	Right	Extracorp. Circulation	Diagnosed by angiocardiography. Well two weeks later.
Chin and Ross	1957	25 M	Left 8 x 7 cm. 60 gm.	Hypothermia	Operated on for mitral stenosis. Survived operation.
Robertson	1957	38	Left 6 cm. diam.	Hypothermia	Surgery for mitral stenosis. Well four months later.
Gerbode co-authors	1958	51 F	Left 42 gm.	Extracorp. Circulation	Diagnosed by angiocardiography.
Ellis (Jly)	1958	45 F	Left 5 x 4 x 4 cm. 34 gm.	Extracorp. Circulation	Surgery for mitral stenosis. Well five months later.
id.	1958	48 M	Right 10 cm.	Extracorp. Circulation	Surgery for mitral stenosis. Well four and one half months later.
Coates, E.	1958	50 F	Right	Extracorp. Circulation	Diagnosed by angiocardiography. Well six months later.
Fatti, L.	1958	45	Left		Surgery for mitral stenosis. Left ventricle incised.
Wittenstein co-authors	1959	22 M	Left 158 gm.	Hypothermia	Operated on for pure mitral insufficiency. Well nine months later.
id.	1959	52 F	Left	Hypothermia	Diagnosed by angiocardiography. Uneventful recovery.
Dugan and Walstad	1959	46 F	Left 8 x 7 x 2½ cm.	Hypothermia	Tumor embolus 1953. Surgery for mitral stenosis 1952. Well 25 months later.

the medial left atrial chamber was removed piecemeal in a period of three and one half minutes. Following closure of the left atriotomy, the procedure was delayed by periods of ventricular fibrillation treated over a 45 minute span with alternate electrical stimulation and cardiac massage. Normal sinus rhythm was eventually resumed and the chest was closed without further difficulty.

Following this operative procedure, she had a much smoother course, except for partial loss of vision on the second postoperative day. Vision was limited to hand movements and light perception. This "blindness" was felt to be due to cortical damage involving the visual cortex from anoxia. The possibility of air embolism was considered.

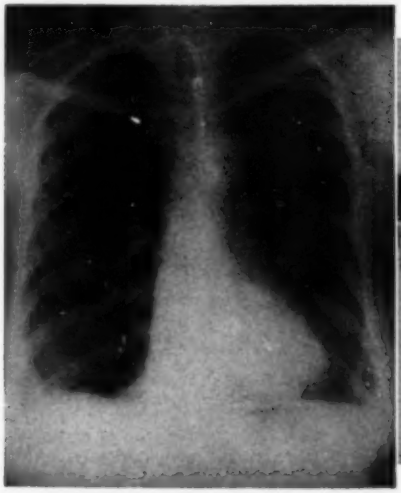
She was returned home on June 7, 1957, two weeks post-operatively, and has been carefully observed for the past two years. Her vision gradually improved over the first five months so that in October, 1957, she was able to read newsprint with glasses. She has had no further embolic phenomena, her cardiac symptoms have disappeared and she is leading an active and normal life. Her last chest roentgenogram in June, 1959, showed normal heart size (Fig. 3).

Pathological Features

The tumor mass removed from this patient measured 8 x 7 x 2½ cms., weighed 43 grams, and presented as a soft, jelly-like mass (Fig. 4). The embolus removed in 1953, and the intracardiac tumor showed similar histologic features. Thorel[10] and Husten[11] have classified these lesions as organized, or degenerate thrombi; however, Ribbert,[12] Mahaim[3] and Prichard[4] hold that these are true neoplasms. Whereas thrombi are usually found in the atrial appendage, myxomas are generally located attached by a pedicle to the interatrial wall in the region of the fossa ovalis with an appendage free of thrombi.

Diagnosis and Treatment

Once the awareness of these tumors is grasped, as in patients considered to have rheumatic heart disease or subacute bacterial endocarditis but showing unusual features, definite diagnostic aids such as angiocardiography should be utilized. The clinical course of such a patient is usually short. Constantly subject to cerebral vascular accidents, multiple



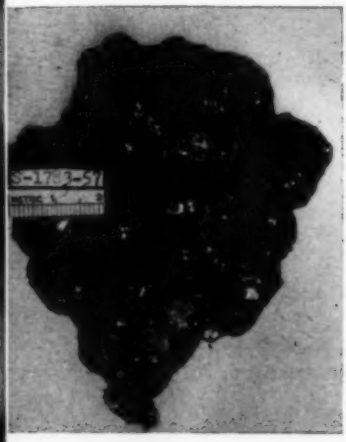


FIGURE 3: Chest film, 1959, showing normal heart configuration.

FIGURE 4: Gross appearance of left atrial myxoma after removal. 8 x 7 x 2.5 cm. in size. Weight: 43 grams.

emboli elsewhere, Stokes-Adams seizures or sudden death, these patients live precariously from day to day.[13,14,15]

Treatment consists of direct visual surgery employing hypothermia or extra-corporeal circulation. As this soft, gelatinous-like growth easily fragments, it is imperative to check for detached tumor fragments in the atrium or ventricle before closing the heart chamber.[16] Tumors found at surgery for mitral stenosis should be done at another time utilizing hypothermia or extra-corporeal circulation, as the hazards of improvising are legion.[17,18,19] At the time of this operation, our only choice of surgical approach to the problem was by means of hypothermia. Experience with a Kay-Cross pump-oxygenator over the past two years has demonstrated to our satisfaction that a case similar to the one presented here would now be best treated with the more leisurely approach afforded by a bypass machine.

Including our case report, there have been 15 reports of successful surgery for intracardiac myxomas (see Table). Diagnosis was made preoperatively in four patients by angiocardiography and in six at operation for suspected mitral or tricuspid valvular disease. Twice as many women as men underwent surgery, the ages ranging from 25 to 61 years. The majority of the tumors arose from the area of the fossa ovalis in the left atrium.

SUMMARY

This is a six year case history of a 46 year-old woman who had successful removal of a myxoma. There was a four year interval between peripheral tumor embolectomy and primary tumor removal.

Cardiac myxomas most often simulate rheu atic heart disease and, to a lesser degree, bacterial endocarditis. Their erratic beh ior can be explained on the basis of mechanical interference with heart action and heir tendency to discharge multiple emboli.

Diagnosis by clinical features only is uncertain so that angiocardiography is being more frequently employed as it tends to show the filling defect created by the tumor.

It is imperative that once the diagnosis is established, surgery be employed.

RESUMEN

Se presenta el caso seguido durante seis años, de una mujer de 46 años de edad a quien se extirpó con éxito un mixoma. Hubo un intervalo de 4 años entre la embolectomía periférica tumoral y la resección del tumor primario.

Los mixomas cardiacos mas a menudo simulan la enfermedad reumática y en grado menor la endocarditis bacteriana. Su evolución caprichosa puede expplicarse por la interferencia mecánica con el corazón y su tendencia a desprender émbolos múltiples.

El diagnóstico por las características clínicas tan sólo es incierto de manera que la angiocardiografía se usa mas frecuentemente ya que tiende a mostrar el defecto de llenado creado por el tumor.

Una vez que se ha establecido el diagnóstico, el tratamiento quirúrgico es imperativo.

RESUMÉ

Il s'agit de l'histoire d'une femme âgée de 46 ans, suivie pendant six ans, qui avait subi une exérèse satisfaisante pour myxome. Il y eut un intervalle de quatre ans entre l'embolectomie de la tumeur périphérique et l'exérèse de la tumeur primitive.

Les myxomes cardiaques simulent le plus souvent un rhumatisme articulaire aigu, et à un moindre degré, une endocardite microbienne. Leur évolution aberrante peut être expliquée par une interférence mécanique avec l'action cardiaque et leur tendance à provoquer des embolies multiples.

Le diagnostic basé uniquement sur les caractéristiques cliniques est si incertain que l'angiocardiographie est de plus en plu fréquemment utilisée car elle tend à mettre en évidence le défaut d'empliссage créé par la tumeur.

Il est impératif de faire appel à la chirurgie une fois le diagnostic établi.

ZUSAMMENFASSUNG

Wiedergabe der sich über 6 Jahre erstreckenden Krankengeschichte einer 46 Jahre alten Frau, bei der ein Myxom mit Erfolg entfernt worden war. Es lag ein Intervall von 4 Jahren zwischen der Entfernung des Primärtumors und der Tumor-Embolektomie im kleinen Becken.

Kardiale Myxome täuschen besonders häufig rheumatische Herzkrankheiten vor, weniger oft auch eine bakterielle Endokarditis. Dieses wechselhafte Verhalten läßt sich erklären an Hand der mechanischen Störung der Herzaktion und der Tendenz, multiple Embolie abzustoßen.

Die Diagnose allein aufgrund klinischer Merkmale bleibt unsicher; es wird deshalb häufiger die Angiokardiographie verwandt, weil sie sich mahr dazu eignet, den durch Tumor bewirkten Füllungsdefekt zu zeigen. Es ist zu fordern, daß operativ vorgegangen wird, sobald die Diagnose feststeht.

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Bilateral Ventricular Hypertrophy Due to Chronic Pulmonary Disease

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Introduction

Eighty autopsy protocols derived from adult men and containing the diagnosis: "Cor pulmonale" have been reviewed at Castle Point, N. Y. In the overwhelming majority of the cases right ventricular hypertrophy was associated with left ventricular hypertrophy; that is to say, the width of the left ventricular wall at its thickest portion exceeded 12 millimeters.

The pathologist, the late Dr. Bernard Barshay had been most careful not to include any trabeculated part of the myocardium or the papillary muscles. The diagnosis of right ventricular hypertrophy was made only when the maximal width of the wall was five millimeters or over. This standard was adopted in the year 1946 arbitrarily and with full knowledge that for adult males the normal value ascribed to the thickness of the right ventricular wall ranged from two to three millimeters. These figures are still considered to be valid.[1]

This presentation is restricted to cases for which the following aspects could be verified by clinical and post mortem data: 1. Presence of chronic pulmonary disease, and 2. Absence of any congenital cardiac malformation, valvular disease, coronary occlusion, myocardial infarction, nephrosclerosis, systemic hypertension, or any medical condition definitely known to cause left ventricular hypertrophy.

Not excluded were cases where the histopathological investigation disclosed microscopic evidence of slight focal replacement fibrosis in the myocardium. Also included were a few records where the autopsy protocol mentioned arteriosclerotic changes of the aorta and the coronary arteries ascribable to physiologic age processes, provided the coronaries had remained patent.

This limited series embraces thirty-two cases. For twenty-seven individuals electrocardiograms were obtained in the absence of digitalis therapy. For five patients electrocardiograms were either not available or had to be omitted from this study in view of a possible drug effect on the tracing. This pertains to cases 4, 5, 11, 21 and 26.

Table 1 shows the age at death, body length, body weight, heart weight and the pulmonary diseases as found on necropsy.

Table 2 shows the abnormal atrial findings on necropsy.

Table 3 shows the thickness of the ventricular walls.

Table 4 shows the left to right ratio for the thickness of the ventricular walls.

Table 5 shows the percentage increase above normal for the thickness of the ventricular walls.

Table 6 shows the electrocardiographic abnormalities as regards the

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axis, the ST segment, the T wave and the QRS complex. On Table 6 the occurrence of the U wave is also listed.

The atrial electrocardiographic findings are summed up in the text.

The study is supplemented by a report of a case with left ventricular hypertrophy without right ventricular hypertrophy. This addition was prompted by an electrocardiographic pattern which conforms with one of the criteria claimed in the literature to be characteristic for right ventricular hypertrophy. The observation was made at the Veterans Hospital, Lyons, N. J., and it is cited in order to emphasize the elusiveness

TABLE 1

Case No.	Age	Height in Inc.	Weight in lbs.	Heart Weight in Grams	Diagnosis on Necropsy
1	56	65½	100	325	Pulm. tbc. Pulm. emphysema.
2	43	Not rec.	130	350	Pulm. tbc. Pulm. emphysema.
3	60	67	140	450	Primary progressive pulm. emphysema. Pulm. tbc.
4	28	65½	150	370	Pulm. tbc.
5	61	66½	145	360	Bronchogenic carcinoma. Pulm. emphysema.
6	34	Not rec.	125	300	Pulm. tbc. Focal. pulm. emphysema.
7	68	66	118	225	Primary progressive pulm. emphysema. Pulm. tbc.
8	53	66	100	365	Pulm. tbc. Pulm. emphysema.
9	52	63	135	275	Pulm. tbc. Silicosis.
10	58	66	170	400	Bronchogenic carcinoma. Pulm. tbc. Pulm. interstitial emphysema. Bronchiectasis.
11	58	60	96	275	Bronchiectasis, Pulm. emphysema. Pulm. fibrosis.
12	50	71	150	550	Pulm. tbc., inactive. Pulm. emphysema.
13	59	Not rec.	131	450	Pulm. tbc., inactive. Pulm. emphysema. Pulm. fibrosis. Bronchiectasis.
14	47	67	140	450	Pulm. tbc. Pulm. emphysema. Pulm. fibrosis.
15	41	Not rec.	115	450	Pulm. tbc. Pulm. fibrosis. Pulm. emphysema.
16	61	69	120	350	Pulm. tbc. Carcinoma of lung. Pulm. emphysema.
17	57	Not rec.	135	400	Pulm. tbc. Pulm. emphysema.
18	57	70	115	400	Pulm. tbc. Pulm. emphysema.
19	59	66	100	400	Pulm. tbc. Pulm. emphysema.
20	53	68	180	550	Pulm. tbc. Bronchiectasis. Pulm. fibrosis. Pulm. emphysema.
21	59	Not rec.	100	425	Pulm. tbc. Bronchiectasis. Pulm. emphysema.
22	59	Not rec.	120	475	Pulm. tbc. Carcinoma of lung. Pulm. emphysema. Pulm. fibrosis.
23	52	60	178	650	Pulm. tbc. Pulm. emphysema. Fibrosis of pulmonary vessels.
24	45	60	Estimated less than 100	400	Bullous pulm. emphysema. Pulm. arteriolar sclerosis.
25	62	69	170	450	Bronchiectasis. Pulm. emphysema. Pulm. fibr. Bronchogenic carcinoma.
26	58	66	110	450	Pulm. tbc. Bronchogenic carcinoma. Pulm. emphysema.
27	58	72	150	550	Pulm. emphysema. Pulm. fibrosis. Bronchogenic carcinoma.
28	64	64	120	360	Pulm. tbc. Pulm. emphysema.
29	37	70	150	550	Primary pulm. atherosclerosis and thrombosis of pulm. arteries. Pulm. emphysema. Pulm. Tbc.
30	48	67	100	375	Pulm. tbc. Pulm. emphysema. Bronchiectasis.
31	52	Not rec.	100	400	Pulm. tbc. Pulm. emphysema. Pulm. fibrosis.
32	47	73	100	400	Pulm. tbc. Pulm. emphysema. Bronchiectasis.

and uncertainty of electrocardiographic criteria for right ventricular hypertrophy.

The age at death of the youngest person was 28 years and the oldest 68 years. The duration of the pulmonary diseases ranged from not less than five years to several decades.

The tabulated data demonstrate the concurrence of bilateral ventricular hypertrophy in protracted and severe pulmonary diseases. It is the author's impression that there is little awareness as regards its existence. This is understandable because a concentric thickening of the myocardium without obvious dilatation of the ventricles will not be identified on the routine chest roentgenogram, when pulmonary emphysema is present.

Among the 32 cases of the series the autopsy revealed pulmonary emphysema in 30, with or without additional pulmonary diseases.

Heart Weight

In order to compare the weight of an abnormal heart with averages deduced from healthy persons one must make the choice between computations based on body height or body weight. Each method of correlation shows a substantial variability as regards the weight of the normal heart. A standard value quoted by Gould[1] reads: "The weight of the normal heart in the adult male is stated to be between 275 and 325 grams."

Among the thirty-two cases of this study there were twenty-seven with the heart weight over 325 grams, as can be seen on Table 1. The weight of the heaviest heart was 650 grams (case 23). The second highest weight was 550 grams, and this applies to four cases (12, 20, 27 and 29).

There was no significant relationship between the weight of the heart and body weight or body height.

Graybiel et al[2] have shown in experiments on dogs that loss of body weight did not influence ventricular weight. In the present series the high heart weights are the expression of a pathological process and they came about irrespective of chronic emaciation and avoidance of physical exertion during prolonged hospitalization, and those conditions applied to an overwhelming majority of patients represented by this investigation.

Atrial Hypertrophy

Out of the 32 necropsies there were six instances where the thickness of the atrial walls exceeded the normal range of 1 to 2 millimeters. These

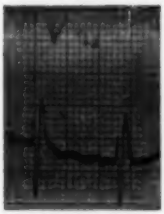

FIGURE 1, Case R15785: Left ventricular hyperthrophy. Delayed onset of the intrinsicoid deflection in lead V_5.

data are shown on Table 2. Three individuals had bilateral atrial hypertrophy and three hypertrophy of the right atrial wall only. The abnormal width of the atrial walls ranged from 3 to 5 millimeters.

Hypertrophy of the Right Ventricle

Table 3 shows the thickness of the right ventricular wall. In the mildest degree of right ventricular hypertrophy the thickness of the right ventricular wall ranged from 3 to 5 millimeters (case 1); and in the severest (case 30) from 10 to 15 millimeters.

Left Ventricular Hypertrophy

Gould quotes Saphir[1] in citing the value for normal thickness of the left ventricular wall, namely 8 to 10 millimeters. Anderson[2] recommends higher figures: 10 to 12 millimeters.

Table 3 shows that the abnormal thickness of the left ventricular wall in the mildest case of cor pulmonale (case 1) measured 10 to 15 millimeters. In the severest case of cor pulmonale (case 30) the left ventricular wall measured also from 10 to 15 millimeters. However, some cases with less right ventricular hypertrophy than the maximal one had a more advanced associated left ventricular hypertrophy (cases 8, 10, 22, 24, 25, 26), the thickness of the left ventricular wall ranging from 15 to 20 millimeters. Left ventricular hypertrophy was absent in one case only (case 2).

The Proportion of Right to Left and Left to Right Ventricular Hypertrophy

For the calculation of the ratio between the thickness of the right and left ventricular walls and vice versa, there were computed the measurements for the maximal width and not the range. The question of interest was: Does increasing right ventricular hypertrophy disclose a quantitatively parallel increase in left ventricular hypertrophy? The figures on Table 4 do not reveal any consistent pattern.

Percentage Increase of Ventricular Thickness Above Normal

As normal thickness of the right ventricular wall the author used again: 3 millimeters, and of the left ventricular wall: 12 millimeters. The thickness of the right ventricular wall shows a percentage increase over normal amounting to 0.66 per cent in the mildest case, and 400 per cent in the severest cases (case 1 versus cases 30, 31, and 32 on Table 5).

The thickness of the left ventricular wall shows a percentage increase over normal amounting to 0.25 per cent in the mildest case of right

TABLE 2 — ATRIAL HYPERTROPHY. THICKNESS OF WALL IN MM.
(Normal Value: 1 to 2 mm.)

Case No.	Right Atrium	Left Atrium
1	2 - 3	2 - 3
12	3 - 4	2 - 3
18	2 - 3	Normal
20	2 - 3	2 - 3
23	1 - 3	Normal
29	3 - 5	Normal

ventricular hypertrophy (case 1 of Table 5) and very variable increases for the whole series, the maximum being 66 per cent (cases 8, 10, 22, 23, 24, 25, 26, 27 and 32).

In relation to the normal values the hypertrophy was very much greater in the right than the left ventricle.

Introduction to the Electrocardiographic Observations

There are elements of incompatibility if not of absurdity in an attempt to correlate electrocardiographic and anatomical findings. For example: It is logical to assume that with the clinical evidence of cor pulmonale the appearance of an abnormal atrial wave, such as a tall peaked P wave, implies distention of the right atrium. However, the in vivo haemodynamic event does not need to be represented in the autopsy by either atrial dilatation or hypertrophy. A dilatation of the atrium may resolve pre mortem or post mortem. Furthermore, in the living individual the position of the atrium may be reflected in the P wave, but that position might not be the same after breathing and cardiac action have ceased.

The following report should be read with these reservations in mind.

TABLE 3 — THICKNESS OF VENTRICULAR WALL
(in millimeters)

Case	Right	Left
1	3 to 5	10 to 15
2	Minimal not recorded — 6	10
3	3 to 6	10 to 15
4	Minimal not recorded — 6	15
5	Minimal not recorded — 6	15
6	5 to 7	10 to 15
7	3 to 7	10 to 15
8	5 to 7	15 to 20
9	3 to 8	10 to 15
10	5 to 8	15 to 20
11	5 to 8	10 to 15
12	5 to 10	10 to 15
13	5 to 10	10 to 15
14	5 to 10	10 to 15
15	5 to 10	10 to 15
16	5 to 10	10 to 15
17	5 to 10	10 to 15
18	5 to 10	10 to 15
19	5 to 10	10 to 15
20	5 to 10	10 to 15
21	5 to 10	10 to 15
22	5 to 10	15 to 20
23	5 to 10	10 to 20
24	5 to 10	15 to 20
25	5 to 10	15 to 20
26	5 to 10	15 to 20
27	5 to 10	10 to 20
28	Minimal not recorded — 12	18
29	8 to 13	10 to 15
30	10 to 15	10 to 15
31	8 to 15	10 to 15
32	8 to 15	10 to 20

The Atrial Wave in Atrial Hypertrophy

This section is devoted to an analysis of the six cases listed on Table 2.

Case 1. Equal bilateral atrial hypertrophy. Twelve days prior to death: peaked P in lead II, 3 millimeters high.

Case 12. Marked bilateral atrial hypertrophy with predominance on the right. One year and eight months prior to death: normal P waves.

Case 20. Equal bilateral atrial hypertrophy. Two months prior to death: normal P waves.

Case 18. Right atrial hypertrophy. One year and six months prior to death: normal P waves.

Eleven months prior to death: slightly peaked P in lead II, 3 millimeters high. The last cited electrocardiogram showed a heart rate of 115, and the tachycardia may or may not have influenced the form and size of the P wave.

Case 23. Right atrial hypertrophy and dilatation. Four days prior to death: normal P waves.

Case 29. The most marked right atrial hypertrophy of the series. One year and five months prior to death: peaked P, lead II, 3 millimeters high. Prominent upright P wave in V_2, 3 millimeters high.

Thus, as regards atrial hypertrophy, there was no consistent correlation between electrocardiographic manifestations and the anatomical findings on autopsy.

The Atrial Wave without Atrial Hypertrophy

Among the twenty-one subjects with electrocardiograms in the absence of digitalis therapy and without atrial hypertrophy there were

TABLE 4 — RATIO FOR THICKNESS OF VENTRICULAR WALLS
(Calculation Based on Values for Maximal Thickness)

Case	Left to Right
1	3.0
2	1.67
3	2.50
4	2.50
5	2.50
6	2.14
7	2.14
8	2.86
9	1.88
10	2.50
11	1.88
12	1.50
13	1.50
14	1.50
15	1.50
16	1.50
17	1.50
18	1.50
19	1.50
20	1.50
21	1.50
22	2.00
23	2.00
24	2.00
25	2.00
26	2.00
27	2.00
28	1.50
29	1.15
30	1.00
31	1.00
32	1.33

fifteen persons whose tracings showed normal P waves. Six had abnormal P waves:

Case 7: Two months prior to the patient's death: P in lead II and lead III and AVF peaked and 3 millimeters high.

Case 14. Sixteen months prior to the patient's death: asymmetric P with a relatively broad descending limb which slants, without a horizontal base line, directly toward the QRS complex in lead II, lead III and AVF. The depth of the descending limb is 3 millimeters. Similar P in V_2, V_3, V_4 and V_5. In AVR the summit of P is flattened and slightly notched.

Case 15. One year and four months prior to the patient's death: P in lead II peaked, 4 millimeters high. Prominent upright P in V_2, V_3 and V_5, 2 millimeters high. Heart shifted to the left.

Case 19. Six months prior to the patient's death: P slightly peaked and 3 millimeters high in lead II, lead III and AVF.

Case 24. One year and 11 months before the patient's death a severe asthmatic attack. Heart rate: 115, P peaked, with deep descending limb, in lead II, lead III and AVF. Prominent P with deep descending limb in V_4. Subsequently, during absence of asthma and with a heart rate of 79, normal P waves, one year and one month prior to the patient's death.

Case 30. Five weeks prior to the patient's death: P peaked, 4 to 5 millimeters high, in lead II, lead III and AVF. Peaked upright P and 3 to 4 millimeters high, in V_5.

TABLE 5 — PERCENTAGE INCREASE OF VENTRICULAR THICKNESS ABOVE NORMAL

(As normal value used for right ventricle: 3 millimeters; as normal value used for left ventricle: 12 millimeters)

Case	Right Ventricle	Left Ventricle
1	0.66	0.25
2	100	No increase
3	100	25
4	100	25
5	100	25
6	133	25
7	133	25
8	133	66
9	166	25
10	166	66
11	166	25
12	233	25
13	233	25
14	233	25
15	233	25
16	233	25
17	233	25
18	233	25
19	233	25
20	233	25
21	233	25
22	233	66
23	233	66
24	233	66
25	233	66
26	233	66
27	233	66
28	300	50
29	333	25
30	400	25
31	400	25
32	400	66

Peaked upright P and 3 millimeters high, in V_1. Peaked upright P and 2½ millimeters high, with descending limb 4 millimeters deep, in V_5. Heart shifted to the left.

Attention is being drawn to the prominent P waves in the precordial leads (cases 15 and 30 with shift of the mediastinum to the left, and cases 24 and 29 without such a cardiac displacement). While with pulmonary heart disease the very rare occurrence of a prominent P wave in the precordial leads has been observed before (Michelson),[4] case 24 is the only instance where the author found this formation to be transient. Such an instability of the P wave supports the concept that acute right atrial dilatation, induced by pulmonary insufficiency, can recede with the abatement of the pulmonary insufficiency.

The clinical aspects of cases 15, 24 and 29 have been reported in a previous publication.[4]

Discussion of the Electrical Axis

With one exception (case 19) all of the electrocardiograms showed right axis deviation.

In view of the bilateral ventricular hypertrophy in this series, the right axis deviation cannot be explained by the effect of a clock wise rotation of the heart on its long axis and a backward displacement of the apex. The autopsy material presented here dispells the notion that right ventricular hypertrophy must achieve or surpass the

TABLE 6 — A. THE ELECTRICAL AXIS

Right axis deviation:	30 patients
No axis deviation:	1 patient
Combination of right and left axis factors with a predominating shift to the right:	1 patient

B. THE rsR' PATTERN

a. *In the absence of a hypertrophied crista supraventricularis:*

1. (Case 18.) QRS in V_2 0.10 second. Onset of r to peak of R' 0.05 second. Duration of the initial r wave 0.02 second. Onset of R' to its peak 0.02 second. R' 8 mm. high.

2. (Case 19.) QRS in V_2 and V_3 0.10 second. Onset of r to peak of R' 0.06 second. Duration of initial r wave less than 0.02 second. Onset of R' to its peak 0.02 second. R' 7 mm. high.

3. (Case 24.) QRS in V_2 0.10 second. Onset of r to peak of R' 0.07 second. Duration of initial r wave 0.02 second. Onset of R' to its peak less than 0.02 second. R' 4 mm. high.

b. *In the presence of hypertrophied crista supraventricularis:*
rsR' pattern absent: cases 3, 12, 13, 14, 23, 30, 31.

C. THE ST SEGMENT

Normal in 20 individuals. Abnormal in 7 individuals.

	II	III	AVF	AVL	V_2	V_3	V_4	V_5	V_6
a. ST depressed	4*	1	1		1	2	1	1	1
b. ST elevated	1	2	1	1					

*The numbers signify the incidence in the various leads for seven individuals.

D. THE T WAVE

Normal in 12 individuals. Abnormal in 15 individuals.

a. *Shallow or isoelectric* — *Shallow, isoelectric or diphasic*

Lead I	Lead II	Lead III	V_1
5**	11	8	1

b. *Inverted*

Lead III	V_1	V_2	V_3	V_4	CF_4
2**	2	5	4	1	1

**The numbers signify the incidence in the various leads for fifteen individuals.

E. THE PROTODIASTOLIC WAVE

Upright U wave present:	6 individuals
absent :	21 individuals

thickness of the left ventricular wall in order to produce right axis deviation. The predominance of the mass of the left ventricular wall over the mass of the right ventricular wall has been demonstrated. Therefore there arises the hypothetical question whether the great muscular performance of the hypertrophied right ventricle may possibly cause an alteration of the electrical potential resulting in right axis deviation.

Discussion of the QRS Pattern

Among twenty-seven patients an abnormal QRS complex was observed in three individuals. An rsR' pattern with a delayed intrinsicoid deflection occurred in V_2 and V_3 without a hypertrophied crista supraventricularis. In contrast to these three instances there was no rsR' pattern and no widening of the QRS complex in the electrocardiograms of seven subjects whose hearts showed on necropsy a hypertrophy of the crista supraventriculars. These observations throw doubt on the concept that the electrocardiographic pattern under discussion is to be regarded as pathognomonic for right ventricular hypertrophy.

At this point an autopsy finding (R-15785, July 3, 1958) at Lyons, N. J., may perhaps be pertinent. The subject's age at death was 59 years. Height: 68 inches. Weight: 90 lbs. History of arterial hypertension. Cause of death: pneumonia. Heart weight: 290 grams. There was left but no right ventricular hypertrophy. The thickness of the right ventricular wall measured up to 3 millimeters and the thickness of the left ventricular wall up to 15 millimeters.

Between the year 1950 and October 1957 eight routine electrocardiograms showed a stable rsR' pattern in V_1 and V_2, the duration of QRS being 0.10 second. There was a delay of 0.06 second in the onset of the intrinsicoid deflection (beginning of r to peak of R'). The duration of the initial r was 0.02 second (this excluding the application of an electrocardiographic classification of "partial right bundle branch block" [Fig. 1]).

Thus, the frequent absence of the delayed intrinsicoid deflection in V_1 and V_2 in the presence of right ventricular hypertrophy and the occurrence of that pattern in association with a normal right ventricle, raise questions as regards the origin and electrocardiographic specificity of that pattern. Is its formation possibly induced or influenced by the activation of the left ventricle?

Discussion of ST Segment

Seven individuals among the series of 27 patients showed abnormalities. They occurred in nine leads as a whole. Hypoxia, associated with pulmonary insufficiency, may be incriminated in the present series because coronary artery disease could be ruled out as a causative factor.

Discussion of the T Wave

Fifteen individuals among the series of 27 patients showed abnormalities. They occurred in eight leads as a whole. Leads two and three were chiefly affected. T_2 was shallow, isoelectric or diphasic eleven times; T_3 was shallow, isoelectric, diphasic or inverted ten times. Inversion of T in V_2 and V_3 summed up to nine instances.

In the opinion of the author these findings are not pathognomonic for cor pulmonale but may be considered as a clue when harmonizing with clinical criteria.

Discussion of the U Wave

The present series of 27 patients with the occurrence of a normal U wave in six individuals is too small for any interpretative attempt.

That the U wave represents "an electrical, i.e. biochemical process occurring during the protodiastolic phase of the heart cycle" has been demonstrated by Groedel and Miller[5] in support of the theory of Maekawa (quoted from Groedel and Miller) who believed the U wave to be a dilatation potential.

Review and Discussion of the Literature

Kounitz, Alexander and Prinzmetal[6] reported in 1936 that among seventeen autopsied cases of pulmonary emphysema there was thickening and dilatation of the right ventricle as well as thickening of the left ventricular wall. From the methodological point of view that study is of great value because the weight of the ventricles was compared after sectioning the heart according to Hermann and Wilson[7] whose material was used for normal controls.

Parker[8] stated in 1940 that a post mortem examination on 32 cases with essential pulmonary emphysema revealed in 11 instances the combination of right and left ventricular enlargement.

While Kounitz and his co-authors could not offer an explanation for their observation, Parker surmised that in his series the work hypertrophy of the left ventricle could be explained most logically on the basis of hypertension in the systemic circulation which was not detected clinically.

Harvey, Ferrer, Richards, Jr. and Cournand[9] declared in 1951: "The left ventricle is not compromised even with chronic cor pulmonale in cardiac failure. There was no enlargement of this chamber radiographically." These authors add that post mortem examinations in eight cases of the investigated series confirmed their impression.

In 1951 Zimmerman and Ryan[10] reviewed 50 cases for cor pulmonale autopsied at Cleveland City Hospital and reported in 1941 by Scott and Garvin.[11] To that series Zimmerman and Ryan added 52 new cases from the same hospital. Zimmerman and Ryan confirmed the findings of Scott and Garvin and stated: "The left ventricle as first reported showed varying grades of hypertrophy. In 93 per cent the left ventricle measured 12 mm. or more and in 41 cases (78 per cent) it measured 15 mm. or more. The cause of this hypertrophy is not clear. However, the recent work of McMichael and Sharpey-Shaffer[12] may tend to elucidate this problem since they showed thta patients with cor pulmonale had increased cardiac outputs which tended to remain elevated even when cardiac failure occurred"

Boettner et al[13] claimed in 1957 that among 38 cases of cor pulmonale the autopsy showed eight cases of dilatation of the left heart. However, this statement is not specified as regards atrial or ventricular location.

While discussing the pathology of cor pulmonale Shepera[14] writes in 1957: "Studies based on ratios of right and left ventricles break down when one considers the recent evidence that the left ventricle may hypertrophy either in sympathy with the enlarging right ventricle or in order to fulfill some function compensatory to the increasing embarrassment of the lesser circulation." He states that a hypertrophy of the left ventricle has been propounded either on an anoxic basis (Spain and Handler)[15] or on the basis of the continuity of the muscle fibre bundles of the right ventricle across the septum to the left myocardium.

Armen, Kantor and Weiser[16] mentioned in 1958 one post mortem case of cor pulmonale in which there was left ventricular hypertrophy without the presence of any other form of heart disease ordinarily leading to increased work of the left ventricle. They write: "Rosenburg and Deenstra[17] have demonstrated the admixture of oxygenated blood in the smaller pulmonary arteries in patients with chronic lung disease, particularly those with bronchiectasis, indicating an extensive collateral circulation from the bronchial arteries. From the standpoint of the left ventricle this mixing represents an arteriovenous shunt and may be responsible for the left ventricular disease."

Another stipulation which was to serve as an explanation for generalized cardiac hypertrophy is the concept of increased myocardial work at certain degrees of low oxygen tensions. In animal experiments this was achieved by Vacek[18] in 1926.

The overstretching of the myocardial fibres has been incriminated as a factor possibly leading to their overgrowth (Best and Taylor).[19]

Cardiac overwork in terms of accelerated heart rate may also be cited among the hypothetical causes for ventricular hypertrophy. From the point of view of the Bainbridge[20] reflex the sequence of the following events is conceivable: a rise of venous pressure in the right atrium, increase of diastolic distention of the cardiac chambers and reflex stimulation resulting in acceleration of the cardiac rate.

The author has seen many patients whose chronic pulmonary insufficiency was associated with myocardial hypertrophy and who did not have sustained tachycardia or any tachycardia prior to sudden or perhaps belatedly identified cardiac decompensation. Among the twenty-seven patients without digitalis therapy the electrocardiograms showed a heart rate ranging from eighty-eight to one hundred fifteen for nineteen patients. The whole group includes a substantial number of persons who have had non-cardiac asthma and concomitant tachycardia periodically during numerous consecutive years. Therefore, tachycardia cannot be dismissed as one of the possible mechanisms contributing to cardiac overwork in chronic pulmonary disease.

It seems to be an established opinion that long lasting and severe pulmonary disease may cause a concentric thickening of the wall of the right ventricle and presumably because this chamber must pump against an increased resistance due to infringement upon the capillary bed.

Among the theoretical considerations for the cause of an associated left ventricular hypertrophy the role of a possible diastolic suction may be stipulated as a hypothesis which merits investigation.

Rushmer[21] writes: "Greater diastolic distension without a corresponding increase in filling pressure may follow administration of epinephrine."

In summing up, the causation of bilateral ventricular hypertrophy in certain patients with chronic pulmonary disease is still an unsolved question.

SUMMARY

A series of 32 necropsy cases with bilateral ventricular hypertrophy due to chronic, severe pulmonary diseases is analyzed.

Three individuals had bilateral atrial hypertrophy, and three right atrial hypertrophy only.

The thickness of the right ventricular wall ranged from 3 to 5 millimeters in the mildest case of cor pulmonale and from 10 to 15 millimeters in the severest case.

The thickness of the left ventricular wall ranged from 10 to 15 millimeters in the

mildest case of cor pulmonale and also from 10 to 15 millimeters in the severest case. However, in several intermediate cases the left ventricular wall measured from 10 to 20 millimeters in thickness.

An arrangement of the cases according to increasing thickness of the right ventricular wall did not disclose a parallel quantitative progression in the left ventricular hypertrophy. This is substantiated by ratios as well as by the percentage increases above normal values, computed for the maximal widths of both ventricles.

For the whole series the hypertrophy was much greater in the right than the left ventricle. For the thickness of the right ventricular wall the percentage increase above normal amounted to 400 per cent in the severest case. For the left ventricle the maximum percentage increase above normal amounted to 66 per cent. However, with the exception of one single case, the absolute thickness of the right ventricular wall was considerably less than the absolute thickness of the left ventricular wall.

The right ventricular hypertrophy was reflected in the electrocardiogram by right axis deviation.

Seven cases with a hypertrophied christa supraventricularis did not show an rsR' pattern in leads V_1 or V_2. Such a pattern with a delayed onset of the intrinsicoid deflection could be demonstrated for a contrast case without right ventricular hypertrophy but with left ventricular hypertrophy.

ACKNOWLEDGEMENT: I wish to express my gratitude to Dr. Albert S. Hyman, Consultant Cardiologist, whose gift of penetrating inquiry stimulated me in my research.

RESUMEN

Se estudia una serie de 32 necropsias de casos con hipertrofia ventricular bilateral debida a enfermedad crónica esvera pulmonar.

Tres individuos tenian hipertrofia bilateral atrial y tres sólo hipertrofia atrial derecha.

El espesor de la pared ventricular derecha varió de 3 a 5 mm. en el caso mas leve de cor pulmonale y de lo a 15 mm. en el caso mas grave.

El espesor de la pared ventricular izquierda tuvo un promedio de lo a 15 mm. en el caso mas leve de cor pulmonale y tambien de lo a 15 mm. en el caso mas severo. Sin embargo, varios casos intermedios mostraron que la pared ventricular izquierda media de 15 a 20 mm. de espesor.

Un arreglo de los casos de acverdo con el aumento de espesor de la pared ventricular derecha no condujo a un aumento cuantitativo parelelo de la hipertrofia ventricular izquierda. Esto es apoyado por las relaciones así como por el porcentaje de aumenot sobre lo normal, estimado por los máximos espesores de ambos ventrículos.

Para todo la serie la hipertrofia fué mucho mayor en el ventriculo del lado derecho que del izquierdo.

Siendo el porcentaje de auemnto del espesor de la pared ventricular derecha de 400 por ciento sobre normal en el caso mas severo. Para el ventriculo izquierdo el porcentaje máximo de aumento sobre lo normal fué de 66 por ciento. Con la excepcion de un solo caso, el espesor absoluto de la pared ventricular derecha fué considerablemente menor que el espesor absoluto de la pared del ventriculo izquierdo.

La hipertrofia ventricular derecha se manifestó en el electrocardiogarma por una desviación derecha axial.

Siete casos con hipertrofia de la cresta supraventricularis no mostraron un forma rsR' en la V_1 ó V_2. Tal cuadro, con un principio retardado de la deflexión intrinsicoide podria ser demostrado por un caso de contraste sin hipertrofia ventricular derecha, pero con hipertrofia ventricular izquierda.

RESUMÉ

L'auteur analyse une série de 32 autopsies de malades atteints d'hypertrophie ventriculaire bilatérale consécutives à de graves affections pulmonaires chroniques.

Trois individus avaient une hypertrophie bilatérale de l'oreillette et trois n'avaient qu'une hypertrophie de l'oreillette droite.

L'épaisseur de la paroi ventriculaire droite variait de 3 à 5 millimètres dans le cas le plus discret de coeur pulmonaire et de 10 à 15 millimètres dans le cas le plus sévère. Cependant, dans plusieurs cas intermédiaires, la paroi ventriculaire gauche mesurait de 15 à 20 millimètres d'épaisseur.

Une classification des cas selon l'augmentation dépaisseur de la paroi ventriculaire droite n'a pas fait découvrir de progression quantitative parallèle de l'hypertrophie du ventricule gauche.

En ce qui concerne la série totale, l'hypertrophie fut beaucoup plus importante pour le ventricule droit que pour le gauche. Pour l'épaisseur de la paroi ventriculaire droite, l'augmentation au-dessus de la normale atteignit jusqu'à 400% dans le cas le plus grave. Pour le ventricule gauche, l'augmentation maximale au-dessus de la normale atteignit jusqu'à 66%. Cependant, à l'exception d'un seul cas, l'épaisseur absolue de la paroi ventriculaire droite fut considérablement moindre que l'épaisseur absolue de la paroi ventriculaire gauche.

L'hypertrophie ventriculaire droite se reflétait dans l'électrocardiogramme par une déviation de l'axe droit.

Dans sept cas comportant une hypertrophie de la crête supra-ventriculaire, il n'y avait pas l'aspect rsR' dans les dérivations V_1 ou V_2. Un tel aspect avec un retard de la déflection intrinsécoïde pourrait être demonstré comme un cas sans hypertrophie ventriculaire droite mais avec hypertrophie ventriculaire gauche.

ZUSAMMENFASSUNG

Eine Serie von 32 Sektionsfällen mit beiderseitiger Ventrikel-Hypertrophie als Folge chronischer schwerer Lungenkrankheit wird ausgewertet. Drei Fälle hatten eine bilaterale Vorhof-Hypertrophie und 3 eine solche des rechten Vorhofes allein. Die Dicke der rechten Kammerwand schwankte zwischen 3 und 5 mm bei den leichtesten Fällen von Cor pulmonale und zwischen 10 und 15 mm bei den schwersten Fällen.

Die Dicke der linken Kammerwand lag zwischen 10 und 15 mm bei den leichtesten Fällen von Cor pulmonale und ebenfalls zwischen 10 und 15 mm bei den schwersten Fällen. Es maß jedoch bei verschiedenen dazwischen gelegenen Fällen die linke Ventrikelwand zwischen 15 und 20 mm.

Eine Anordnung der Fälle nach zunehmender Dicke der Wand der rechten Kammer offenbarte keine parallele quantitative Progression der Hypertrophie der linken Kammer. Es wird dies erkenntlich sowohl durch die Verhältniszahl, als auch durch den prozentuale Anstieg über die Normalwerte, errechnet für die maximale Wandlicke beider Ventrikel.

In der ganzen Reihe war die Hypertrophie viel größer am rechten als am linken Ventrikel. Was die Dicke der Wand der rechten Kammer angeht, so erreichte der prozentuate Anstieg über die Normalwerte bis zu 400% bei den schwersten Fällen. Beim linken Ventrikel kam es zu einem maximalen prozentualen Anstieg über die Normalwerte bis zu 66%. Mit Ausnahme eines einzigen Falles war jedoch die absolute Dicke der rechten Kammerwand beträchtlich geringer als die absolute Dicke der linken Kammerwand.

Die Hypertrophie des rechten Ventrikels äusserte sich im EKG in einer Abweichung der rechten Achse. Fälle mit einer hypertrophierten christa supraventricularis zeigten bei den Ableitungen V_1 oder V_2 keine rsR' Zeichen. Ein solcher Ablauf mit verzögertem Beginn der wesentlichen Zacke konnte in einem Kontrastfall ohne Hypertrophie der rechten Kammer-aber mit Hypertrophie der linken Kammernachgewiesen werden.

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Angina and the Amine Oxidase Inhibitors*

The story of the amine oxidase inhibitors and angina starts with the serendipitous discovery by Cesarman[1] that iproniazid (Marsilid), the prototype of the group, dramatically relieved anginal pains in cardiac patients being treated for depression. This was confirmed by Master[2] and others,[3] who recognized the toxic as well as the salutary effects on patients with angina.

Mechanism of Action

While knowledge of the mechanism is not complete, it is known that many enzymatic reactions are affected in vitro and in vivo, and a major action of this group of drugs is described by their name — amine oxidase inhibitors.

Firstly, an amine is a derivative of ammonia (NH_3) in which one or more of the hydrogens has been replaced by an organic radical. Among the important amines of the body affected in this instance are norepinephrine and serotonin.

Secondly, an oxidase is an agent which catalyzes an oxidative reaction — in this case, the oxidation of norepinephrine and serotonin in certain body cells — the brain, nerve cells, heart and liver, in particular.

Thirdly, an inhibitor is an agent which acts to prevent a reaction. The prevailing theory is that this group of drugs prevents the usual oxidation of norepinephrine and serotonin with a resultant uninhibited buildup of these undestroyed amines in the cells of certain parts of the brain, the liver, and the heart.

The time it takes for the buildup of amines roughly approximates the time it takes for Marsilid to decrease the pains of angina pectoris, usually from three to ten days.[4]

At present, the brain and nerve cells appear to be the main site of action. Angina pectoris is a psychosomatic manifestation. In accordance with this concept, Griffith[5] recognizes that contributing to the patient's general feeling of well-being is of great importance in the therapy of the patient with angina. On the other hand, the significance of the peripheral buildup of norepinephrine, in the myocardium is not clear, and reports on change in coronary flow contradict each other. There is no evidence that Marsilid causes a specific reversal of the primary pathologic process.

The Evaluation of Antianginal Agents

The proper evaluation of an antianginal agent by decrease in frequency of attacks of chest pain must take into consideration that angina pectoris is paroxysmal chest pain of psychosomatic origin with little

*Presented in part at the Homecoming Meeting, American College of Chest Physicians, Albuquerque, New Mexico, October 14-17, 1959.

consistent quantitative relation to the underlying coronary disease. Marsilid does affect the psyche, but has not been shown to affect the coronary disease process underlying angina pectoris. In addition to the specific action of the antianginal agent, decrease in frequency may be due to placebo effect, spontaneous remissions and fluctuations in the course of angina, and finally, may result from the effect of good physician-patient relationship which is established in the rapport period, the first two to eleven weeks of treatment.[6] These factors may be circumvented by employment of the double-blind technique, and utilization of multiple control periods in the post-rapport interval. To further prevent error, Katz[7] has suggested that each patient in the series be subjected, also, at several different times, to both the drug and the placebo.

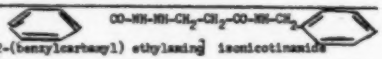
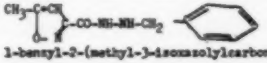
Shoshkes and associates[8] met these stringent resuirements in testing Marsilid, and found it "to be effective in relieving the pain of a total of 64 per cent and 73 per cent of the patients respectively on two separate periods, while the placebos were effective in only 30 per cent on two separate periods. These differences analyzed statistically were shown to be significant. The effects of Marsilid were plainly cumulative as evidenced by an increasing rate with time, of both therapeutic effect and of untoward reaction."

Toxicity of Marsilid

The serious toxic effects fall into three categories — those due to overdosage, resulting in overstimulation of mental and physical activity, and manifestations of orthostatic hypotension, those due to potentiation of the action of other drugs such as the barbiturates and chlorothiazide. Lastly, and most serious, is hepatitis — that is a hepatocellular type of liver damage that is difficult to distinguish from viral hepatitis.

Among the minor toxic effects are dryness of the mouth, flatulence, constipation, difficulty in micturition, impotence, blurring of vision, dizziness, twiching, euphoria, and insomnia. Because of the toxicity of Marsilid, over 300 of its less toxic analogues are being studied.

TABLE 1 — NAMES AND STRUCTURES OF THE AMINE OXIDASE INHIBITORS

NAME		
Trade	Other	Chemical Structure
Marsilid	Iproniazid	 1-isonicotinyl 2-isopropyl hydrazine
Niamid*	Nialamide	 N-[2-(benzylcarbamyl) ethylamino] isonicotinamide
Marplan**	Isocarboxazid MO-5-0831/1	 1-benzyl-2-(methyl-3-isoxazolylcarbonyl) hydrazine
Catron***	Phenylisopropyl-hydrazine JB-516	 B-phenylisopropylhydrazine
Nardil****	Phenelzine W-15Ah	 B-phenyl-ethyl hydrazine

Marsilid Analogues

Four of the less toxic amine oxidase inhibitors have reached the stage where they can be used, under careful medical superivision, for patients with severe angina.

Marplan,[9] Catron,[9] and Niamid,[10] each have been reported to produce marked to moderate improvement in more than 70 per cent of patients with angina. Nardil[11] is said to be similarly effective. In anginal patients with radioiodine-produced hypothyroidism the addition of Niamid has permitted larger doses of thyroid to be administered with fewer attacks of chest pain.

A double-blind study is in progress to compare the antianginal effect of the four amine oxidase inhibitors against each other, and a long acting nitrite, Cardilate.[12]* So far it is apparent that Marplan and Catron have a salutary effect over and above long-acting nitrites, in that patients who did not mind when the nitrites were discontinued, insistently demanded the return of the amine oxidase inhibitor which had so greatly relieved them of anginal pain.

In the words of a patient who had received many other medications over a two year period, "This is the first medicine that really works!" When the pains returned to another patient following reduction of Marplan dosage from 30 to 20 mg. a day, she made a special trip to the hospital to have the original 30 mg. of Marplan restored. This episode illustrates the principle that the precise effective daily dosage of the amine oxidase inhibitors must be adjusted carefully for each individual. Since these preparations have a cumulative effect, the dose should be reduced promptly as soon as clinical improvement is observed. A small initial amount followed by gradual increases to the effective dose may avoid toxic effects.

Side effects from the iproniazid analogues have been minimal, consisting of postural hypotension, dizziness, insomnia, and jitteriness. They have been controlled by reducing the dosage. To date jaundice or hepatitis has not occurred in this series.[13] Pre-existing hepatic damage is a contraindiction to the use of all the amine oxidase inhibitors; one case of hepatitis has been reported.[13]

The amine oxidase inhibitors are effective adjuvants to the treatment of severe angina pectoris. Certainly they should not be used indiscriminately, without close medical supervision which should include: proportionate restriction of activity; frequent estimations of standing blood

*Cardilate brand Erythrol Tetranitrate sublingual tablets and identical placebos provided through courtesy of Burroughs Wellcome & Co., (U.S.A.) Inc.

TABLE 2 — DOSAGE OF THE AMINE OXIDASE INHIBITORS. DAILY INITIAL AND MAINTENANCE AMOUNTS.

DRUG	Daily Dose in Milligrams	
	Initial	Maintenance
Marsilid	150	25— 200
Marplan	30	5— 40
Catron	12	3— 9
Niamid	75	37.5— 150
Nardil	45	15— 75

pressure to forestall postural hypotension; liver function tests such as serum bilirubin and transaminase tests to detect early hepatitis; and electrocardiograms to uncover infarctions which the relief of pain may have concealed. The search continues for the least toxic amine oxidase inhibitor and for the most effective antianginal agent.

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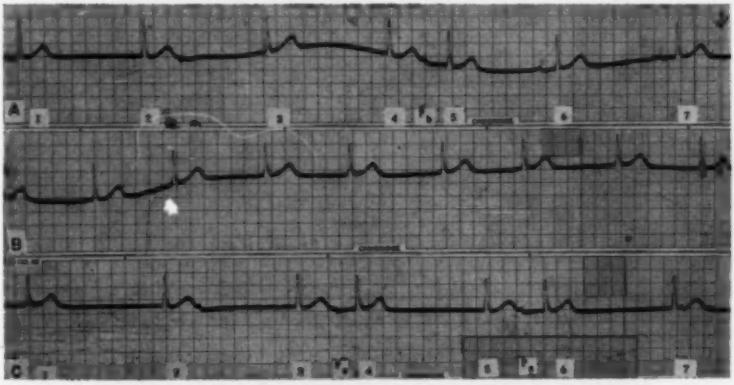
ELECTROCARDIOGRAM OF THE MONTH

Reciprocal Rhythm with an Unusually Long R-R Interval

In strip A, the first four beats are of AV nodal origin in the pattern of AV dissociation with an R-R interval of 1.8 seconds. The second QRS complex is followed by an inverted P wave due to retrograde depolarization of the auricle; the other beats have retrograde block. The fourth complex is followed by an upright sinus P wave which produces a "ventricular capture" i.e. the fifth QRS complex. This is followed by two beats with sinus rhythm. The second strip B of this continuous record of Lead II manifests a regular rhythm (R-R of 1.16 seconds), first degree heart block and an ectopic auricular focus with a P contour unlike the sinus



beats or retrograde AV nodal P waves. In the lower strip, C, the AV nodal pacemaker becomes dominant again. Complex 2 has a sinus P wave superimposed upon the T waves but beat three is followed by a retrograde P wave and an R-P interval which is 0.05 seconds longer than the R-P interval of the second complex in strip A. This permits the re-entry of the auricular stimulus into the AV junctional tissue and produces a reciprocal beat (complex four), an inverted P wave "sandwiched" between two QRS complexes and an R-R interval of 0.89 seconds. The next coupled sequence consists as it did in strip A of an AV nodal beat (beat 5) with retrograde block followed by an upright sinus P wave and a ventricular capture (beat 6) with a P-R interval of 0.36 sec.

It has been stated that reciprocal rhythm may be diagnosed when the two ventricular complexes occur within 0.5 seconds of each other. This case demonstrates a remarkably long R-R interval in the reciprocal rhythm complex. Coupled beats four and five of strip A and five and six of strip C are good examples of "pseudoreciprocal rhythm." This abnormal tracing appeared in a patient with ischemic heart disease, and was not related to drug effect.

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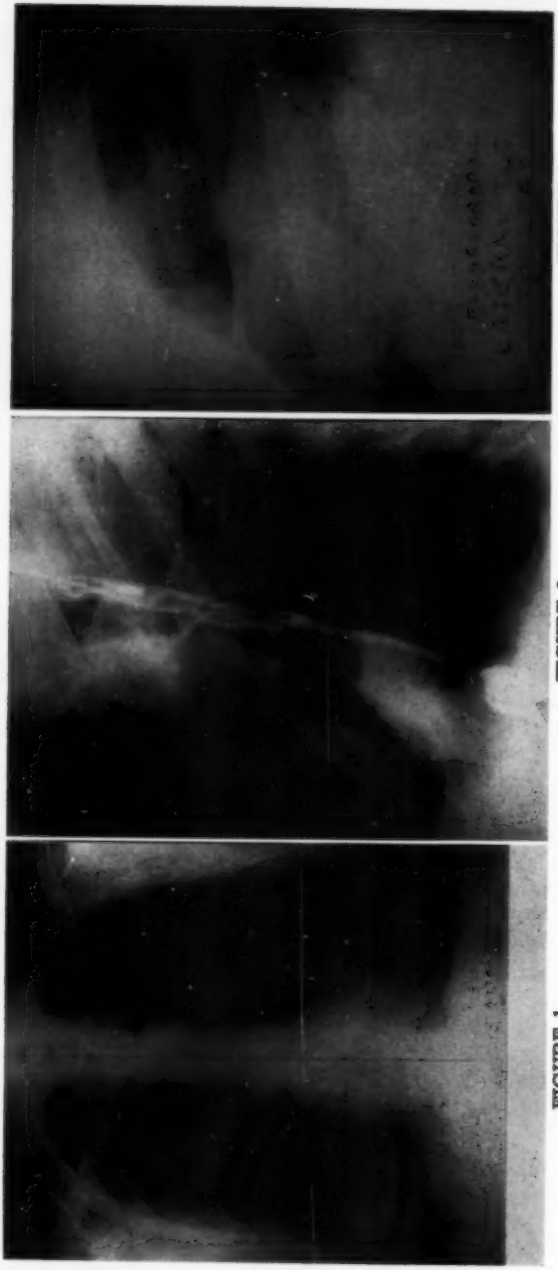

FIGURE 3

FIGURE 2

FIGURE 1

The patient was a 55 year-old white man who gave a history of an episode of hemoptysis eight days before examination. Following this, blood streaked sputum persisted. Physical examination demonstrated only roughening of the breath sounds in the right lung, in the right axillary region.

Answer

X-ray film examination of the chest showed a large cyst in the anterior inferior portion of the right lower lobe involving the anterior basal segments. The anterior wall of the cyst was adjacent to the interlobar septum between the right middle and lower lobes. The cyst showed an air fluid level with its lower two-thirds filled with fluid. The superior portion of the cyst wall was thin and linear. Inspiratory-expiratory studies demonstrated marked compressibility of the cyst. In the mid-portion of the air fluid level there was a 3 cm. soft tissue mass. Fluoroscopically, this changed position with tilt of the patient, indicating that it was floating on the surface of the fluid. This strongly suggested that the fluid within the cyst was blood and that a blood clot was floating upon it.

Exploratory thoracotomy showed a subpleural cyst involving the anterior basal segments of the right lower lobe. The cyst was filled with blood. A resection of the cyst was performed. Microscopically, its wall showed no evidence of an epithelial lining.

Pulmonary cysts are subdivided into:

1. Alveolar or emphysematous cysts
2. Bronchiogenic, bronchopulmonary or congenital cysts
3. Cystic bronchiectasis
4. Specific cysts

By definition, the bronchiogenic cysts should be lined by bronchial epithelium. Cysts are found, however, which grossly appear to be bronchiogenic in nature, yet microscopically have no epithelial lining. It is possible that these are bronchiogenic cysts, but that their wall had been altered by pressure or infiltration. The above described cyst may have these characteristics.

Hemorrhage is much more frequent in bronchiogenic than in alveolar cysts. It may be caused by injury to the chest wall, even minor in degree. The roentgen demonstration of a mobile soft tissue mass associated with an air-fluid level is usually indicative of blood clot. Only a well defined oval density will be seen if the bronchi are not patent. A blood filled cyst will occasionally rupture into the pleural cavity producing a spontaneous hemopneumothorax.

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The Committee on Chest Roentgenology welcomes comments. We would also be pleased to receive x-ray films of exceptional interest with brief history. Please submit material to: Benjamin Felson, M.D., chairman, Department of Radiology, Cincinnati General Hospital, Cincinnati, Ohio.

North American Blastomycosis of a Nasal Sinus:

REPORT OF A CASE

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Houston, Texas

Introductory Remarks

North American blastomycosis is an infection caused by the hypomcete, *Blastomyces dermatitidis,* and is characterized by suppurating and granulomatous lesions of the skin, subcutaneous tissues, lungs, bones (particularly the vertebrae and ribs), liver, spleen, kidneys, and the central nervous system. Most of the cases of North American blastomycosis have been reported from the United States, especially from Louisiana, North Carolina, Wisconsin, Illinois, Kentucky, Ohio and Tennessee, listed in order of frequency. Each of the original 48 states has reported a small number of cases excepting Idaho, Nevada, Arizona and New Hampshire.

The organism occurs in nature and, although doubtless from an exogenous source, is not contagious. A few cases have presumably been caused by direct inoculation or prolonged contact with an infected individual. In systemic blastomycosis, the lung is the most frequently infected organ.

The objective of this paper is to report a proved case of infection of the nasal antrum with *Blastomyces dermatitidis,* with extension into the left orbital cavity. A careful survey of the domestic and foreign literature has uncovered only one such observation, by O. Czurda,[1] of North American blastomycosis of a maxillary antral sinus. The signs and symptoms of this patient conformed closely to those of mine in that smears and cultures revealed budding fungi characteristic of North American blastomycosis, the nasal cavity was free of infection, and there was definite limitation of mobility and dual vision of the homolateral eye. Our case, therefore, seems to be the first one reported from the Western Hemisphere, at least, and the second instance of such an infection found in medical literature.

Case Report

Mrs. R. W., aged 36 years, white, farm wife, was admitted to the Greer Clinic on June 19, 1957, complaining of severe, dull pain over the left maxillary antrum and left orbit, protrusion of the left eye, dual vision, and a sensation as though the eye were being pushed upward and outward. The present complaints included a slight cough, a small amount of mucoid expectoration, a 30-pound loss in weight, weakness, extreme fatigability, and temperature varying from normal to 100° F. She was born near Gatesville, Texas and had never been out of the state. The family history was entirely irrelevant. She was referred to me by Dr. Fred Hodde of Brenham, Texas after a surgical exploration of the left maxillary antrum by Dr. Lyle J. Logue of Houston had revealed a thick granulomatous mass completely filling it. An histopathological report of the tissue from the left antrum was inconclusive, although the possibility of a fungal or tuberculous infection was suggested.

No record of cultures was made at this time. Subsequently, she received installations of 2 per cent gentian violet into the left maxillary antrum two or three times each week. An x-ray film of her lungs made at Milroy Hospital in Brenham, Texas, by

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*Presented at the 25th Anniversary Homecoming Meeting, American College of Chest Physicians, Albuquerque, New Mexico, October 17, 1959.

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Dr. Robert R. Haaskarl was interpreted as follows: "The left lower lung lobe shows diffuse increased density, infiltrative-like, with several small, poorly circumscribed, translucent lesions and mottled densities. There is an ovoid cavity about 1½ x 2½ cm. near the mid-zone at about the 8th and 9th ribs on the posterior level, and some evidence of regional pleural thickening. The left hilar zone has some increased density and descending bronchial trunks yield accentuated shadows. The apex of the right lung, the parenchyma, hilar area, bronchial pattern, pleura and diaphragm, all do not appear exceptional. The cardiomediastinal outline is regular in conformation, location and size. The large thoracic vessels are negative. The heart is in upright position. No neoplastic process is recognized."

It was shortly after the foregoing investigation that the patient was referred to me.

Past History: Mrs. R. W. stated that she had been in good health until about 14 years previously when she was awakened at night by severe coughing and wheezing, and choking sensations, with expectoration of yellowish thick sputum — all of which lasted about one hour. There was no fever. This attack was diagnosed as asthma, for which she was treated for some time. Her symptoms continued, with intervals of complete freedom from illness for periods as long as three months. Her episodes were always worse late at night, especially during cold, damp weather. About 10 years previously, she had had slight hemoptysis on one occasion. Several times her antra were punctured, releasing a discharge of gummy, brown-colored material. She was sent to another clinic where her antra were opened, after which she felt somewhat better for a short time. She began to have a great deal of pain over the frontal and antral sinuses in 1943, and it continued until 1947. She was examined again in 1948, and was given penicillin for three weeks, but failed to improve. Following this examination, she continued to have antral washings, but still complained of coughing, wheezing and expectoration of viscuous, thick yellow sputum until she was referred to me.

Dr. Logue re-opened her left antrum at my request on July 24, 1957, to obtain tissue for biopsy and bacteriologic study. The histopathologic report, as given by Dr. Peter Marcuse of Houston, Texas, was, in part, as follows: "a granulomatous process presenting in the form of epithelioid cells, leukocytes and multinucleated giant cells. These elements were arranged within compact, rounded granulomatous foci . . . . necrosis in some areas, but no true caseation is encountered. Many of the giant cells contain well-defined, rounded structures, and some also present elongated septate elements suggestive of hyphae . . . . . are evidently of fungus origin. . . . . A specific organism cannot be demonstrated in spite of the presence of fungi within the giant cells . . . . . bacteriologic studies reveal Penicillium and Aspergillus and it is plausible to assume these organisms were within the infected sinus." (Note: It is to be remembered that the patient received washings of her antrum with gentian violet several times a week for many weeks before this biopsy was made.)

Physical Examination: She was a large, heavily-boned woman, 6 feet, 1 inch tall, weighing 146 pounds, T. 99° F., P. 100, R. 20, blood pressure: systolic 118; diastolic 78. The left eyeball was quite prominent and rotated upward and outward, and the conjunctiva was deeply injected and edematous. There was a moderate amount of periorbital edema and exquisite tenderness over the left orbit and the left antrum. There was considerable yellowish, purulent discharge from the left nasal cavity, but no lesion was found therein. The smears and cultures were positive for Staphylococcus aureus, but negative for *Blastomyces dermatitidis*. On physical examination, Mrs. W. appeared to be quite ill, weak and depressed. Chest examination revealed depressed

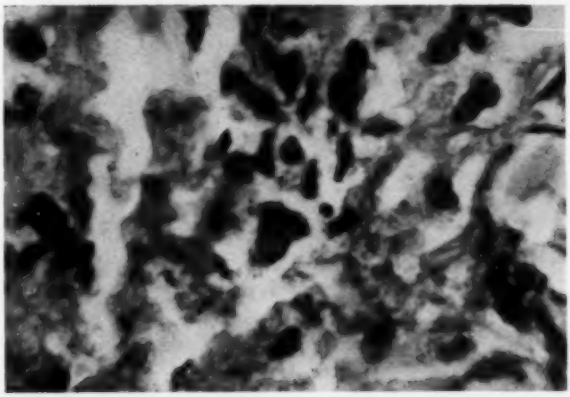

FIGURE 1: Photomicrograph of a section taken from the left antrum, July 25, 1957, shows double-contoured yeast-like cells, budding yeast-like cells, segmented cells and hyphae. Periodic—Acid-Schiff Stain; X 1900.

breath sounds in both bases, particularly on the left, associated with crepitant rales in the left basal area. The remainder of the physical examination was uninformative. There was a moderate hypochromic anemia. The urinalysis was normal. The intradermal tests for tuberculosis, histoplasmosis, blastomycosis, coccidioidomycosis and brucellosis were negative. Smears and cultures of tracheal and gastric washings ,nasal exudate and bone marrow were uninformative. X-ray film of the chest presented slightly increased markings throughout the right upper lobe of the lungs, but nothing suggestive of a disease process. In the left basal area, ranging from the hilum downward and outward, extending almost to the diaphragm and to the left lateral wall of the chest, was a rather hazy density, approximately 2 x 3 cm. in diameter, in the center of which was a small area of cavitation.

After examining the tissue from the left antrum in our laboratory, it was our opinion that the double-contoured, budding, yeast-like cells and segmented cells indicated an infection with *Blastomyces dermatitidis* and that the Aspergillus and Penicillium fungi previously reported were contaminants which developed between the time of surgery and the time the tissue was fixed. A specimen was submitted to Doctors Norman F. Conant and David T. Smith of Duke University at Durham, North Carolina, for study and opinion. They commented as follows: "The section contained double-contoured, yeast-like cells, budding yeast-like cells, segmented cells and hyphae. In our opinion these were all *Blastomyces dermatitidis*. The unusual appearance of the segmented growths and hyphal forms in tissues can be explained by the growth of organisms during the period when the tissue had been allowed to stand at room temperature before it was fixed. The cavity in Mrs. W.'s lung may be due to her secondary infection with B. staphylococci. We have found a number of such cases." Biopsy specimens were also submitted to Dr. Franz Leidler, Pathologist, Memorial Hospital, Houston, Texas, for study, together with pathological slides from the biopsy of July 24, 1957. Dr. Leidler reported as follows: "These slides show active tubercles containing fungi. My impression of the lesion is in keeping with that expressed in the report from Duke University. It is quite obvious that the disease was highly active at the time of the original biopsy." Biopsy material obtained from the left antrum early in September, 1957 was submitted to Dr. Leidler for further examination. He divided the biopsy tissue into four portions from the opening of the sinus, and his findings were as follows:

"Tissue submitted: 1. Sinus. 2. Scar at surgical opening into sinus.

"Gross: The specimen consists of multiple small fragments of tissue from the sinus. #1, from within the sinus; #2 scar tissue at the opening into the sinus. A representative amount is taken for section. The biopsy taken for study by this laboratory consists of two parts. One part represents scar tissue from the surgical opening into the sinus. This part is identified with the number 2. Histologically, a rather uniform fi-

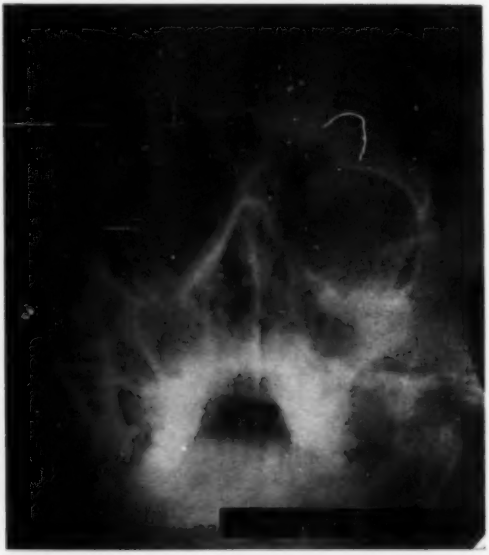

FIGURE 2: Roentgenogram of nasal antral sinuses, October 14, 1957. Both nasal sinuses are opaque. There is a destructive lesion connecting the left antrum with the lower and mesial portion of the left orbit, and generalized hazy opacity of the orbital cavity.

brous tissue with surface squamous epithelium is seen. Here and there indifferent collections of lymphocytes, plasma cells, and polymorphonuclears are present. No evidence of a granulomatous lesion comparable to that seen in the original biopsy can be found in the scar tissue. The second part of the present specimen consists of fragments of mucosa curetted from the sinus. For the most part, there is an inflammatory reaction of a polymorphonuclear type. One larger fragment, however, shows significant changes. In it, the residues of a nodular lesion with giant cells are encountered. Clear-cut tubercles such as those seen in the original biopsy can no longer be identified. As several levels are examined, some of the giant cells are found to contain elements which stain very poorly in hematoxylin-eosin preparation but could be thought of as poorly preserved fungi. Gridley stain of the same area indeed shows clearly identifiable round bodies, as well as fragments of hyphae. The deficient staining qualities of these fungi suggest loss of viability.

"Bacteriologic Study: The biopsy material is divided so that portions of both the scar tissue from the opening to the sinus and of the sinus contents are submitted for bacteriologic study. The study is directed toward identification of the fungus. Multiple tubes and plates of Thompson's blood medium and Sabouraud's medium are inoculated and incubated at 37° and room temperature. In addition, four mice are inoculated intraperitoneally with ground tissue from the sinus. This material is suspended in broth containing penicillin. The direct cultures are negative six weeks after inoculation. The mice did not show signs of clinical disease. Two weeks after inoculation they were skin tested for sensitivity to blastomycin. Three of the mice showed a slight reddening of the test site as compared to the control site. This reaction was doubtful. The three mice were sacrificed. They did not show gross lesions. Peritoneal washings were inoculated on to the above mentioned culture media and were incubated at room temperature and at 37° C. Growth of bacteria and of non-pathogenic yeast was obtained. No pathogenic fungus was cultured after three and one half weeks of incubation.

"Comment: The histopathologic picture is that of a sclerosing granuloma with residual recognizable fungi. When compared to the original lesion, this picture identified a tendency toward healing by fibrosis. In itself, this observation does not prove elimination of active infectious agents. In combination with the negative cultures and the negative mouse inoculations, however, the findings can reasonably be assessed as evidence for arrest of this patient's sinus infection."

"Diagnosis: Maxillary sinus, fungus granuloma (compatible with blastomycosis, see St. Joseph's Surgical 57-3915-B) Histologic arrest of granuloma by fibrosis."

The patient was admitted to the Milroy Hospital, Branham, Texas, on September 4, 1957 and, under the joint care of Dr. Fred Hodde of Brenham and the author, was given 2-hydroxystilbamidine intravenously for a period of 26 days. Six weeks after the end of the first course, the treatment was repeated. Her improvement was remarkable. She gained weight; the previously marked exophthalmos and facial edema disappeared; the nasal cavity was dry; and all subjective symptoms ceased. The intra-

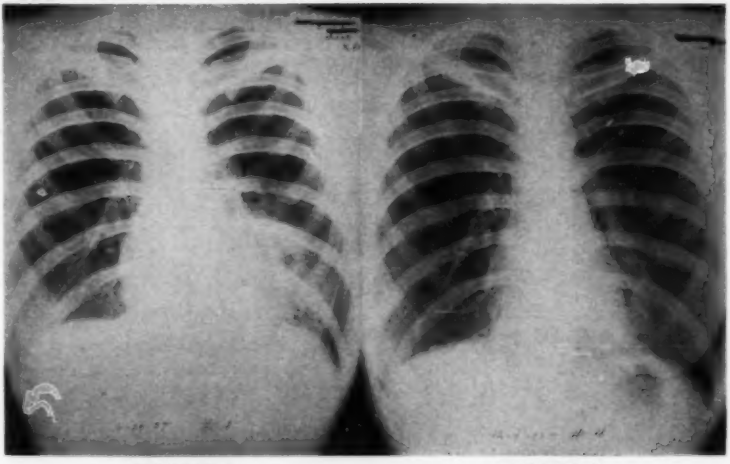

FIGURE 3 FIGURE 4

FIGURE 3: Roentgenogram of chest, June 24, 1952, reveals diffuse mottling in the left lower lung field, extending from the left hilum to just above the left diaphragm. Within the above described area is a small area of rarefaction suggestive of cavitation at the junction of the left mid-clavicular line and the anterior fifth rib.

FIGURE 4: Roentgenogram of chest, December 4, 1958, showing clearing of findings described in Figure 2.

dermal blastomycin test was negative on September 28, 1957. A chest x-ray film made October 14, 1957 was entirely negative for signs of pulmonary pathology. Complement fixation tests, October 25, 1957, were positive in a dilution of 1:16 for blastomycin, but negative for coccidioidin and histoplasmin. On the same day the nasal sinuses revealed moderate opacity.

She was referred to Dr. E. L. Goar for his opinion regarding her eye condition. His report was as follows: "She had a unilateral exophthalmos which measures R. 16 mm., L. 20 mm., and some involvement of the extraocular muscles so that she had diplopia in certain directions of gaze. Vision was good and there was no involvement of the optic nerve or retina." A second examination was made by Dr. Goar on January 24, 1958, and his comments are as follows: "The vision in her right eye is 20/20 and in the left eye, 20/20 without correction. She still has some exophthalmos. It measures with the Hertel ophthalmometer, R. 17, L. 24. The left eye is decidedly higher than the right, measuring 14 prism diopters of left hypertropia. She cannot move the left eye down and outward properly, nor can she rotate it outward to the left canthus. This indicates that something is interfering with the inferior rectus muscle, and slightly with the left rectus. This probably is due to fibrosis following the infection in her sinus. She is annoyed with double vision somewhat because of this, but does not complain severely about it. There is no indication whatever of a lesion of the fundus of either eye."

The patient's condition continued to improve until April 9, 1958, when she developed measles, and her symptoms recurred. She returned to the Clinic on April 23, 1958, exhibiting severe exophthalmos of the left eye, which was tender and edematous. X-ray film of the left antrum showed definite opacity with extension into the left orbital space. The chest x-ray film was negative. Sedimentation rate, 1 hr., 29 mm.; C-reactive protein, 2+; moderately severe hypochromic anemia; erythrocytes, 3,500,000; leukocytes, 5,000; hemoglobin, 11.2 grams; polymorphonuclear cells, 66; stabs, 2; small lymphocytes, 33; monocytes, 1; eosinophils, 4. Biopsy material obtained from the left antrum, smears, cultures and bone marrow studies were all negative.

She was admitted to Memorial Hospital, Houston, Texas, on April 23, 1958, and one week later Amphotericin B was begun. She received a total of 890 mg. of Amphotericin B during a period of 21 days. Her course in the hospital was uncomplicated except for moderate nausea and fever.

During the period of treatment, the complement fixation titer for blastomycin varied from the original 1:16 positive, gradually decreasing throughout 1958 to 1:4 until on July 3, 1959, it was 1:1. Intradermal tests with blastomycin, coccidioidin and histoplasmin were regularly and consistently negative.

On May 28, 1958, Mrs. W. was discharged from the hospital, and from that time until June 1960 she has shown no sign or symptom of recurrence of her fungus disease. There is no nasal discharge or protrusion of the left eye, but a slight outward and upward deviation of the left eyeball remains, and at times there is dual vision. She came to the Clinic on June 6, 1960, complaining of an abscess at the inferior portion of the left lower eyelid. The left eye was somewhat rotated to the left and upward. The abscess was aspirated and cultures were made on blood agar at 30°C and 37°C. Both cultures were positive for Blastomyces Dermatitidis in pure cultures. Her skin tests for blastomycosis, histoplasmosis, and coccidioidomycosis were negative. She was placed in Memorial Hospital and given 50 mg. of Amphotericin B. intravenously. After the sixth treatment the abscess was dry and the outward and upward deviation of the left eyeball disappeared completely. Her treatment is being pursued by her home physician, Doctor Fred Hodde, of Brenham, Texas under my supervision.

Discussion

The second case of North American blastomycosis of a nasal sinus appearing in both foreign and domestic literature has been reported. The initial response to 2-hydroxystilbamidine was excellent but the mycotic infection recurred approximately five months after the termination of the second course of the drug. It would seem that she has recovered following the use of Amphotericin B, although she still has a 1:1 positive complement fixation test. It is our decision to watch for any retrogression of her condition and not attempt further therapy.

ACKNOWLEDGMENT: The author is grateful to Doctors David T. Smith and Norman F. Conant of Duke University, Doctors Franz Leidler, Peter Marcuse, Everett L. Goar and Lyle J. Logue of Houston, and Dr. Fred A. Hodde of Brenham, Texas for their assistance with this case.

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Cystic Disease of the Lung with Acquired Systemic Pulmonary Shunt*

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Cystic disease of the lung combined with an arteriovenous shunt is not common. The case reported in which this association was noted was of further interest in that the shunt was an acquired one from the systemic to pulmonary venous circulation.

Case Report

M. J., an 18 year-old pregnant housewife, was initially seen by her referring physician on July 7, 1958 when he noted a systolic murmur in the second anterior interspace just to the left of the sternal border, in the course of a routine prenatal examination. He then obtained a roentgenogram of the chest (Fig. 1) which revealed a cystic area off the left anterior segment, containing a small fluid level.

A history was given of a slight, non-productive cough. There had been recurrent respiratory infections throughout childhood, but she was free of any complaints when seen. The history relative to her pregnancy suggested that she was in her fifth month of gestation.

The physical examination on admission was within normal limits with the exception of the finding of a well-localized systolic murmur with a low pitched diastolic component located just to the left of the sternal border in the second anterior interspace, which was not transmitted. The murmur was found to be obliterated on Valsalva maneuver. There was absence of clubbing of the fingers and no cyanosis was noted. The pulmonary second sound was not accentuated. The blood pressure in the arms was 115/35 and in the legs 140/75/60 mm. Hg. The pulse rate was 100 per minute.

Complete hematologic studies, blood chemical studies, urinalysis and electrocardiograms were within normal limits. Skin tests were positive only to histoplasmin. There was no polycythemia. Repeat roentgenograms of the chest on July 25, 1958 (Fig. 2) revealed that the previously noted cystic area of the left upper lobe (Fig. 1/ had become converted into a homogeneous density suggesting that drainage of the cystic space was blocked. The lesion seemed to be confined to the anterior segment and there was no evidence of pulsations about the area on fluoroscopic examination. At bronchoscopy on August 12, 1958, only thin mucoid secretions were found issuing from the left upper lobe bronchus.

On August 25, 1958 left thoracotomy was performed and the findings (Fig. 3) were of multiple cystic areas presenting on the mediastinal surface of the anterior segment of the left upper lobe. The area betwen the arch of the aorta and the pulmonary

*From the Department of Thoracic Surgery Baptist Memorial Hospital.

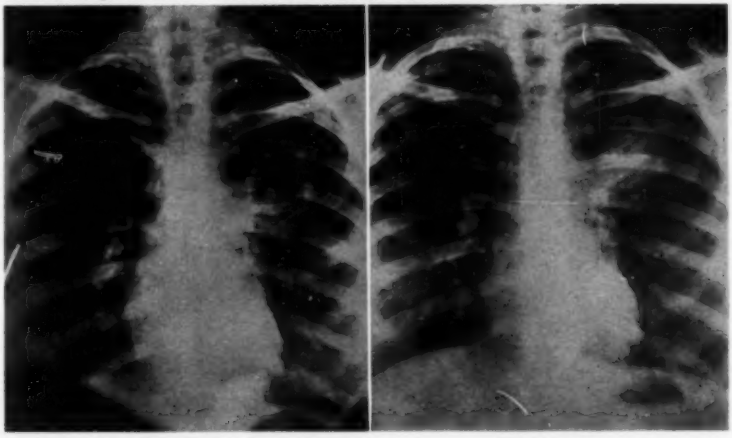

FIGURE 1 FIGURE 2

FIGURE 1: Posterioanterior roentgenogram of June 8, 1958, showing a cystic area containing a small fluid level projecting from the left hilar shadows. FIGURE 2: Posterior-anterior roentgenogram of July 22, 1958, showing a homogeneous density replacing the cystic area seen in Fig. 1.

artery was negative for evidence of a patent ductus arteriosus. There were large, tortuous arterial channels arising from the pericardiophrenic artery averaging 4 to 5 mm. in diameter which ramified into the involved area and connected by extensive collateral channels to the segmental veins draining this segment. The pericardiophrenic artery itself measured approximately 4 mm. in diameter. After interrupting these arterial channels and resecting the anterior segment, the bruit was obliterated. A normal artery was found leading to the anterior segment during the dissection of the left pulmonary artery.

The specimen consisted of a large cystic mass composed of three large communicating cysts having an average diameter of 2 to 2.8 cm. each. The cysts were filled with a viscid, grayish to yellow, purulent material. There were numerous tortuous vascular channels averaging 3 to 4 mm. in diameter which were more prominent near the medial aspect of the specimen.

On microscopic examination, the specimen consisted of cystic masses containing purulent material and lined by bronchial type epithelium. There was smooth muscle in the walls, but no cartilage was found. The blood vessels in the fibrotic interstitial tissue (Fig. 4) were abnormally large and numerous. The arteries were sclerotic and the veins showed considerable irregular, eccentric subintimal sclerosis. These vessels were of sufficient size, were abnormally numerous and were in abnormally close proximity, all of which suggested the existence of an abnormal collateral arteriovenous bed. Therefore a final diagnosis of "Cystic disease of the lung with an acquired, collateral arterio-venous bed" was made.

She had an uneventful convalesence and was discharged from the hospital September 5, 1958.

Discussion

The scattered, discrete, calcified lesions noted in all chest x-rays (Figs. 1 and 2) were thought to represent healed histoplasmosis. The lesion of the anterior segment of the left upper lobe was diagnosed as congenital cystic disease, but no completely satisfactory explanation for the bruit was found. In the differential diagnosis, patent ductus arteriosus, pulmonary arterio-venous fistula and an acquired systemic-pulmonary arterial shunt was considered.

This lesion suggested a bronchopulmonary sequestration of the lung, but had certain features which served to set it apart. The lesion occurred in the left upper lobe and many authors have described bronchopulmonary sequestration[2,3,4] as commonly occurring in the lower lobes and only rarely elsewhere. Then, there was communication with the bronchial tree in this case which is reported as occurring infrequently. The origin of the aberrant vessel in this case was quite different from those most often described, arising from the pericardiophrenic artery on the left rather than directly from the descending thoracic or abdominal aorta as earlier mentioned by Haight,[5] though in certain instances there have been cases reported[6] of the anomalous vessel arising directly from a major, primary branch of the aorta. In no instance, in the literature reviewed, has an account of an anomalous vessel arising from the pericardiophrenic artery been found. Finally, and in this case, of most interest the anomalous vascular communication is apparently acquired rather than congenital

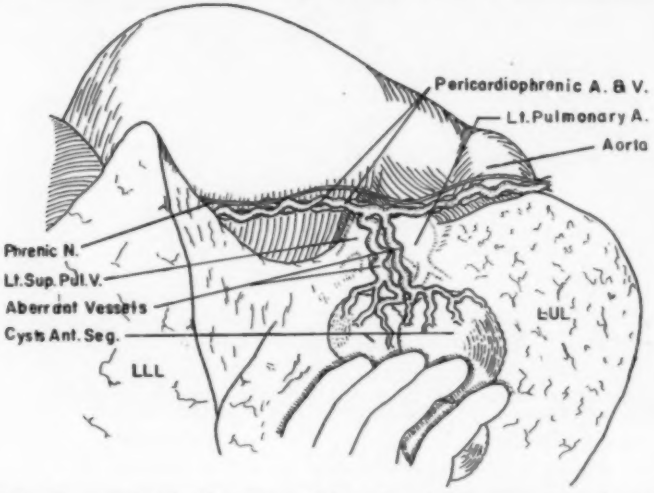

FIGURE 3: Diagram illustrating the pathology found at surgery. Note the size of the pericardiophrenic vessels.

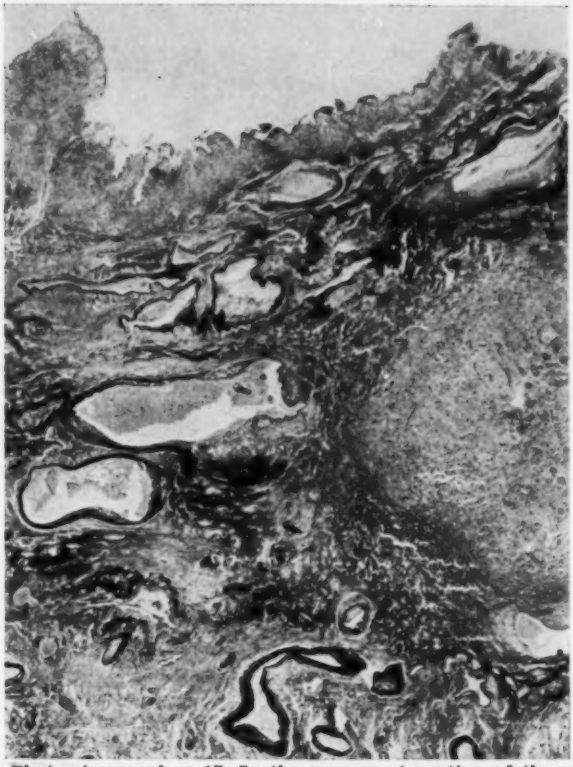

FIGURE 4: Photomicrograph x 17. In the uppermost portion of the specimen is a fragment of bronchial epithelium from a cyst wall, immediately beneath which are large vascular channels. In the far right margin is a small abscess.

as the lung was found to be intimately adherent to the pericardium in this area, being bound by dense, vascular adhesions. This indicated that with repeated inflammatory episodes within the cystic area, as the lung became adherent to the pericardium, vascular communications were established, which, once established, gradually increased in size until they were of sufficient magnitude to produce the bruit heard over the left anterior chest wall. Since the communication consisted of a shunt from a systemic artery to pulmonary segmental veins, the picture of pulmonary arteriovenous fistula, viz. cyanosis, polycythemia, clubbing of fingers and arterial unsaturation did not occur.

The finding on microscopic examination of cysts lined by bronchial epithelium, having smooth muscle, but lacking in cartilage are representative of bronchiolar cysts. The finding of abnormally numerous, large and intimately arranged arterial and venous channels with sclerosis, supports the gross findings suggesting an acquired systemic-pulmonary collateral arterio-venous bed.

ACKNOWLEDGMENT. We are indebted to Dr. T. C. Gladding of the Department of Pathology, Baptist Memorial Hospital, Memphis, Tennessee for his study and confirmation of the pathologic nature of this lesion.

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Transition from Tuberculosis to Sarcoidosis*

RAYMOND SESHUL, M.D., and DONALD J. GRUBB, M.D.
Alexandria, Louisiana

The development of tuberculosis in patients afflicted with sarcoidosis has frequently been noted, but the transition from tuberculosis to sarcoidosis rarely has been reported. The following case report is being presented as an illustration of such a transition.

C. S., a colored man, was 31 years of age when first admitted to the Veterans Administration Hospital, Alexandria, Louisiana, in 1944 as a transfer from the Armed Forces with a diagnosis of tuberculous prostatitis and seminal vesiculitis. This diagnosis was confirmed by cultural methods. At that time, the tuberculin test was positive and the x-ray film of the chest was negative. Sputum studies for acid-fast bacilli by smear were negative as were cultures of the sputum and gastric washings. Between 1944 and 1958 this patient had eight admissions to this hospital. During that interval, tuberculosis recurred in other sites, but the lungs were not involved. Tuberculosis was confirmed in each instance by cultural methods. In 1947, tuberculosis of the spine was found and he became paraplegic. Following drainage of the tuberculous abscess, the paraplegia disappeared and he became ambulant. In 1950, the last spinal fusion was done. In 1951, a draining sinus which communicated with the right fifth costal cartilage was excised. Anti-tuberculosis chemotherapy consisting of streptomycin, paraaminosalicylic acid and isoniazid, was used between 1950 and August, 1957 when chemotherapy was discontinued on the advice of an internist at the Veterans Administration Regional Office, Houston, Texas. Numerous x-ray films of the chest during these years were negative as were the sputum and gastrict cultures for acid-fast bacilli. He was relatively asymptomatic between August, 1957 and September, 1958 when he reported for a routine check-up at the Veterans Administration Regional Office, Houston, Texas. Following the advice received at the Regional Office, he reported to the Veterans Administration Hospital, Alexandria, Louisiana, in October, 1958 for his ninth admission allegedly to rule out meningitis.

On admission, his only complaint was an occasional headache which had been present for three to four weeks prior to admission. The headaches were described as dull, retrobulbar, and invariably occurred late in the evening following reading or watching television. The headaches were quickly relieved with aspirin and were not associated with nausea, vomiting, or stiffness of the neck nor accompanied by fever, chills, night sweats or anorexia.

Physical examination revealed a well developed and nourished colored man, age 45, who did not appear acutely or chronically ill. Walking was done slowly and in a guarded manner with the aid of a cane. A back brace was being used. The entire back was stiff and motion nil in all directions as a result of spinal fusion. The right testicle was absent due to previous surgery. The neurological examination was normal. Examination of the heart, lungs, abdomen, head, neck and eyes showed no abnormalities. There was no lymphadenopathy.

Laboratory studies revealed the initial white blood count to be 3,250 with a normal differential count. Several additional counts were similar. Hemogram otherwise was normal. Liver and kidney function studies were normal. Total protein 7 grams per cent with albumin 4.4 grams per cent and globulin 2.6 grams per cent. A serum protein analysis by electrophoresis showed 45.3 per cent albumin and 54.8 per cent globulins, the latter distributed as follows: Alpha 1, 5.3 per cent; Alpha 2, 10 per cent; Beta 17.5 per cent; and Gamma 22 per cent. Repeat uric acid values ranged between 5.2 and 5.3 mgm. per cent. Calcium studies normal. Smears of sputum and gastric cultures were negative for acid fast bacilli. Guinea pig negative for tuberculosis after 60 days. Cultures and guinea pig inoculation with material obtained from sternal marrow and scalene lymph node were negative for acid fast bacilli. Sputum cultures and complement fixation tests for fungi were negative. Mantoux skin test positive 15 mm. induration. Bronchoscopy negative. X-ray films of hands and feet were negative for cystic changes. X-ray film of the chest revealed bilateral hilar adenopathy which had not been noted previously. Heart shadow and lung fields were within normal limits. Several additional chest films showed little change although slight decrease in adenopathy may have occurred (See Figures 1, 2 and 3). X-ray films of the spine revealed fusion extending from the seventh thoracic vertebra to the sacrum. Micro-

*From the Medical Service, Veterans Administration Hospital, Alexandria, Louisiana.

FIGURE 1 FIGURE 2 FIGURE 3

FIGURE 1: Representative postero-anterior film of chest taken in 1960. Earlier films not available. Negative chest. FIGURE 2: Postero-anterior film of chest taken in 1958 shortly prior to development of hilar adenopathy. FIGURE 3: Postero-anterior film of chest revealing hilar adenopathy not previously demonstrated. Subsequent films essentially unchanged.

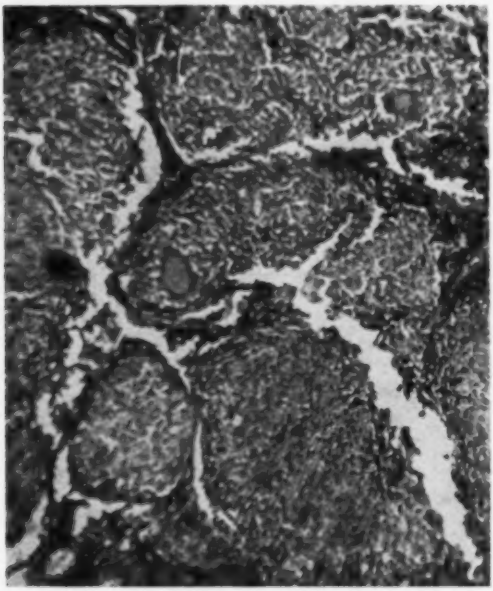

FIGURE 4: Typical sarcoid reaction with giant cell formation and absence of central caseation.

scopic examination of a scalene lymph node was compatible with Boeck's sarcoid. These slides were reviewed independently by three pathologists who made the same interpretation (See Figure 4).

During the six months of hospitalization he was asymptomatic and afebrile. Following initiation of cultural studies, prophylactic therapy consisting of isoniazid and streptomycin was given. Steroid therapy was entertained, but not given on the advice of the area consultant in chest disease who felt that the patient was improving satisfactorily without steroids. He was discharged with instructions to be rechecked at two month intervals. The findings would support the concept that sarcoidosis developed upon an arrested case of tuberculosis.

ACKNOWLEDGMENT: We wish to thank Dr. John S. Chapman, Veterans Administration Area Consultant in Chest Disease, for his advice and helpful suggestions. We also wish to thank the following pathologists who reviewed the microscopic slides: Dr. Esmond Ray Long, formerly with Phipps Institute, Dr. Edward Uhrich, Baptist Hospital, Alexandria, Louisiana, and Dr. Justin Martin, Veterans Administration Hospital, Alexandria, Louisiana.

CHAPTER NEWS

PACIFIC NORTHWEST CHAPTER

The annual meeting of the Pacific Northwest Chapter of the College will be held at the Olympia Hotel, Seattle, Washington, November 11 and 12. The following program will be presented:

Friday, November 11

12:00 noon Buffet Luncheon
Welcome and Introduction
Edward H. Morgan, Seattle, Chapter President
Panel discussion: "Progress in Intracardiac Surgery"
Moderator: G. Hugh Lawrence, Seattle
Panel: Peter Allen, Vancouver, Canada
Ralph Berg, Spokane
Dean Crystal, Seattle
William R. Rumel, Salt Lake City, Utah
Albert Starr, Portland, Oregon
Afternoon Session—Franklin R. Smith, Seattle, Chairman

2:00 p.m. "Value Grafts: Present Status and Future Possibilities"
Lester R. Sauvage, Seattle
Discussion: Albert Starr, Portland, Oregon
"1960 Concepts of Obstructive Pulmonary Disease"
John Martin, Seattle
Discussion: Frederick Casserd, Seattle
"Carbon Dioxide Narcosis"
August C. Swanson, Seattle
Discussion: John Martin, Seattle
"Aortography to Distinguish Vascular Abnormalities from Chest Tumors"
J. Karl Poppe, Portland, Oregon
Discussion: Robert H. Rosenberg, Seattle
"Cobalt 60 in Pulmonary Carcinoma"
Thomas Carlile and Edward H. Morgan, Seattle
Discussion: William R. Halliday, Seattle
"Surgical Implications of Suppurative Lung Disease"
Donald R. Burke, Seattle
"Experimental Considerations of Pulmonary Hypertension"
George M. Bogardus, Seattle

6:30 p.m. Social hour

8:00 p.m. Dinner—Guest Speaker: Edward Allen Boyden, Seattle
"Sir Astley Cooper and the Medical London of His Time"

Saturday, November 12

8:00 a.m. Breakfast and business meeting
Morning Session—J. Karl Poppe, Portland, Oregon, Moderator

9:00 a.m. "In-Hospital Care of Infants of Tuberculous Mothers"
G. W. J. Fiddes, Prince Rupert, Canada
Discussion: Thomas Sheehy, Seattle
"Hyaline Membrane Syndrome"
C. Warren Bierman, Seattle
Discussion: Donald M. McIntyre, Seattle
"Percutaneous Catheterization for Study of Left Heart Valves and Coronary Arteries"
Melvin M. Figley, Seattle
Discussion: Leon Phillips, Seattle
"Use of Radioactive Krypton for the Diagnosis of Congenital Heart Disease in a General Hospital"
Jay C. Michel, Seattle
"Left Atrial Myxoma Simulating Pure Mitral Stenosis" (motion picture)
George I. Thomas, Gordon Logan, Frank J. Jarvis and William K. Edmark, Seattle

1:30 p.m. Homecoming Football game—University of Washington vs. California

NEW ENGLAND STATES CHAPTER

The New England States Chapter will hold its fall scientific meeting at the Sheraton Plaza Hotel, Boston, November 18 and 19, in conjunction with the meetings of the Massachusetts Society of Internal Medicine and Regional Section of the American College of Physicians. The chapter will present the following program:

Friday, November 18

6:00 p.m. Registration and social hour

7:00 p.m. Dinner

8:30 p.m. Scientific Session—David P. Boyd, Boston, presiding
"Lung Cancer - Cigarette Controversy"
Clarence Cook Little, New York City
Ernest L. Wynder, New York City

Saturday, November 19

8:30 a.m. Registration

9:00 a.m. Scientific Session—Peter F. Harrington, Providence, Rhode Island, presiding
"Recent Advances in Functional Evaluation of the Lungs"
Edward A. Gaensler, Boston
Discussion: James A. Bougas, Boston
"Ambulatory Treatment of Pulmonary Tuberculosis"
Samuel Clive Cohen, Boston
Discussion: Emil Rothstein, Brockton, Massachusetts
"Arteriovenous Fistulae of the Lung"
Lewis Haynes, Capt., MC, USN
Discussion: George Starkey, Boston
"Cineradiography in the Diagnosis of Congenital Heart Disease"
Thomas Forsythe, Providence, Rhode Island
Discussion: Edward D. Neuhauser, Boston

10:25 a.m. Intermission

10:30 a.m. Francis M. Woods, Boston, presiding
"Recent Advances in Acquired Heart Disease"
Dwight E. Harken, Boston
Discussion: Lester L. Vargas, Providence, Rhode Island
"Recent Advances in Congenital Heart Disease"
Robert E. Gross, Boston
Discussion: Paul F. Ware, Worsester, Massachusetts
"Thymectomy for Myasthenia Gravis"
Henry Viets, Brookline, Massachusetts
Discussion: David P. Boyd, Boston

12:00 noon Business meeting

COMMITTEE ON NOMINATIONS

The 27th Annual Meeting of the College will be held in New York City, June 22-26, 1961. The members of the Committee on Nominations for offices to be elected in 1961 are:

Donald R. McKay, Buffalo, New York, Chairman
Elected by the Board of Regents

Alexander Libow, Miami Beach, Florida
Elected by the Board of Governors

Henry C. Sweany, Mt. Vernon, Missouri
Appointed by the President

Recommendations for elective offices may be addressed to: Dr. Donald R. McKay, 1275 Delaware Avenue, Buffalo, New York. The Committee on Nominations will meet in Washington, D.C. on November 28, 1960, during the Interim Session of the College.

COMMITTEE ON SCIENTIFIC PROGRAM FOR 1961 ANNUAL MEETING REQUESTS ABSTRACTS OF PAPERS

New York City will be host to the 27th Annual Meeting of the College, June 22-26, 1961. Plans for the scientific program are under way and physicians interested in presenting papers are invited to submit a 200-word abstract in triplicate to the Committee on Scientific Program for consideration. These should be addressed to the Executive Offices of the College, 112 East Chestnut Street, Chicago 11, Illinois. Abstracts submitted on or before November 15, 1960 will be reviewed by the committee when it meets in Washington, D.C. on November 28, 1960.

John F. Briggs, St. Paul, Minnesota
Chairman, Section on Cardiovascular Diseases

H. S. Van Ordstrand, Cleveland, Ohio
Chairman, Section on Pulmonary Diseases

COMMITTEE ON MOTION PICTURES

The Committee on Motion Pictures of the College is interested in learning of new films on diseases of the chest (heart and lungs) for possible presentation at the 27th Annual Meeting of the College in New York City in June. All pertinent information concerning films may be forwarded to Dr. Paul H. Holinger, chairman of the committee, 112 East Chestnut Street, Chicago 11, Illinois. Those accepted for presentation in the annual motion picture program will be eligible for the 1961 Film Contest and will be referred to the judging committee for review. The Committee on Motion Pictures will also be pleased to review films for official approval and inclusion in the Approved Film List of the American College of Chest Physicians.

COLLEGE INTERIM SESSION AND SEMI-ANNUAL MEETING, BOARD OF REGENTS

The Shoreham Hotel, Washington, D. C. will be headquarters for the Interim Session of the College, November 26-27. The Clinical Meeting of the American Medical Association will be held in Washington, November 28 - December 1 at the National Guard Armory. For hotel reservations, please write to the Shoreham Hotel in Washington, indicating arrival and departure dates and that you will attend the meeting of the American College of Chest Physicians.

Dr. Joseph W. Peabody, Jr., Washington, D. C., Chairman of the Scientific Program Committee, has announced the following program arranged by his committee and which is sponsored by the Potomac Chapter of the College. The popular round table luncheon discussions and fireside conferences are included in the program. An ADVANCE REGISTRATION AND RESERVATION FORM may be found on page 472 of this issue. Members planning to attend the meeting are urged to complete this form at once and forward it to the Executive Offices of the College in Chicago. Your badge, program, and luncheon and banquet tickets will be awaiting your arrival at the College Registration Desk in the Shoreham Hotel.

SATURDAY, NOVEMBER 26

Morning Session

8:30 a. m. — REGISTRATION

8:55 a. m. — SCIENTIFIC SESSION

Co-Chairmen: **M. Jay Flippe,** Miami, Florida, President, American College of Chest Physicians

Robert H. Parrott, Washington, D. C., Medical Director, Children's Hospital

9:00 a. m. — Symposium on Congenital Bronchopulmonary Disorders

Inborn Errors of Metabolism as a Potential Source of Chronic Bronchopulmonary Disease

Paul E. A. di Sant'Agnese, Clinical Professor of Pediatrics, Georgetown University School of Medicine, Washington, D. C.

Bronchopulmonary Sequestration

Howard A. Andersen, Consultant in Medicine and Thoracic Diseases, Mayo Clinic, Rochester, Minnesota

Congenital Abnormalities of the Pulmonary Arteries

Milton V. Davis, Assistant Clinical Professor of Thoracic Surgery, University of Texas Southwestern Medical School, Dallas, Texas

Congenital Versus Acquired Lung Cysts: An Important Distinction

Willis J. Potts, Surgeon-in-Chief, Children's Memorial Hospital, Chicago, Illinois

Foregut Anomalies as a Cause of Respiratory Disease

Sol Katz, Chief, Medical Service, Mt. Alto Veterans Administration Hospital, Washington, D. C.; Joseph W. Peabody, Jr., Clinical Assistant Professor of Thoracic Surgery, Georgetown University School of Medicine, Washington, D. C.

Breathing Problems Related to Anomalies of the Great Vessels

Lt. Colonel Hu A. Blake, MC, Chief, Thoracic Surgery Service, Walter Reed General Hospital, Washington, D. C.

11:00 a. m. — PANEL DISCUSSION:

Present Place of Palliative Procedures in Congenital Heart Disease

Moderator: **Bernard J. Walsh,** Associate Clinical Professor of Medicine, Georgetown University School of Medicine, Washington, D. C.

Panel: **J. Frank Damman,** Associate Professor of Surgical Cardiology, University of Virginia Medical School, Charlottesville, Virginia

Willis J. Potts, Surgeon-in-Chief, Children's Memorial Hospital, Chicago, Illinois

Frank C. Spencer, Associate Professor of Surgery, John Hopkins University School of Medicine, Baltimore, Maryland

12:30 p. m. — ROUND TABLE LUNCHEON DISCUSSIONS

A-1 BRONCHITIS: ITS PREVALENCE AND RELATIONSHIP TO AIR POLLUTION

Alvan L. Barach, Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons, New York City.

Albert Roberts, Chief, Clinical Investigation, Air Pollution Medical Program, U. S. Public Health Service, Washington, D. C.

Moderator: **Richard A. Prindle,** Chief, Air Pollution Medical Program, Division of Public Health Services, Washington, D. C.

A-2 HIATAL HERNIA: THE QUESTION—WHEN SHOULD SURGERY BE ADVISED?

William S. Lyons, Clinical Instructor in Thoracic Surgery, Georgetown University School of Medicine, Washington, D. C.

David C. H. Sun, Chief, Gastroenterology Section, Mt. Alto Veterans Administration Hospital, Washington, D. C.

Moderator: **Herman J. Moersch.** Director of Medical Education and Research, American College of Chest Physicians, Chicago, Illinois.

A-3 POSTMYOCARDIAL INFARCTION SYNDROME

Benjamin Manchester, Assistant Professor of Medicine, Georgetown University School of Medicine, Washington, D. C.

Joseph K. Perloff, Director, Diagnostic Laboratories, Division of Cardiology, Georgetown University School of Medicine, Washington, D. C.

Moderator: **William Dressler,** Chief of Cardiology, Maimonides Hospital; Consultant in Cardiology, Brooklyn Hospital, Brooklyn, New York

NOTE: Seating capacity at the round table luncheons is limited and reservations will be accepted in the order received. Please complete coupon on page 472.

Afternoon Session

1:55 p. m. — SCIENTIFIC SESSION

2:00 p. m.—Some Practical Lessons in Cardiology

Co-Chairmen: **George F. Evans,** Past-President, Potomac Chapter, Clarksburg, West Virginia
Robert T. Kelley, Clinical Assistant Professor of Medicine, Georgetown University School of Medicine, Washington, D. C.

Clinical Features of Severe Pulmonary Stenosis in Infancy: A Potential Surgical Emergency

Cdr. John J. Dempsey, MC, USN; Lt. John H. Mazur, MC, USN; Lt. Cdr. Gerald I. Shugoll, Cardiology Service, National Naval Medical Center, Bethesda, Maryland

Clinical Features and Operative Management of Hypertrophic Subaortic Stenosis

Edwin C. Brockenbrough, Senior Assistant Surgeon; Eugene Braunwald, Chief, Section of Cardiology; Andrew G. Morrow, Chief, Clinic of Surgery, National Heart Institute, Bethesda, Maryland

Management of the Severe Acute Hypertensive Episode

Harold W. Schnaper, Assistant Chief, Medical Service, Mt. Alto Veterans Administration Hospital, Washington, D. C.

Helpful Clinical Inferences from Bedside Observation of the Jugular Pulse

Joseph K. Perloff, Director, Diagnostic Laboratories, Division of Cardiology, Georgetown University School of Medicine, Washington, D. C.

Newer Emergency Measures in Cardiorespiratory Resuscitation: An Appraisal of Mouth-to-Mouth Breathing, External Cardiac Massage, External Defibrillation, Postoperative Respiratory Support and Post-Resuscitative Hypothermia

Frank C. Spencer, Associate Professor of Surgery, John Hopkins University School of Medicine, Baltimore, Maryland

3:50 p. m.—*The Problem of Pulmonary Hypertension*

Co-Chairmen: **John F. Briggs,** Associate Professor of Clinical Medicine, University of Minnesota Medical School, St. Paul, Minnesota
W. LeRoy Dunn, Senior Attending in Medicine, Washington Hospital Center, Washington, D. C.

Clinical Recognition of Pulmonary Hypertension

Thomas W. Mattingly, Director of Medical Education, Washington Hospital Center, Washington, D. C.

Etiologic Aspects and Therapeutic Prospects

J. Frank Damman, Associate Professor of Surgical Cardiology, University of Virginia Medical School, Charlottesville, Virginia

SUNDAY, NOVEMBER 27

Morning Session

8:55 a. m.—*Symposium on the Role of Steroid Therapy in Chest Diseases*

Co-Chairmen: **Hollis E. Johnson,** Nashville, Tennessee, President-Elect, American College of Chest Physicians

J. Winthrop Peabody, Sr., Past-President, American College of Chest Physicians, Washington, D. C.

9:00 a. m.—*Bronchospastic States*

Alvan L. Barach, Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons, New York City

Diffuse Pulmonary Infiltrations

A. E. Anderson, Jr., Attending Internist, Baptist Memorial Hospital, Jacksonville, Florida

Severe Life-threatening Pulmonary Infections

Mark H. Lepper, Professor and Head, Department of Preventive Medicine, University of Illinois College of Medicine, Chicago, Illinois

Sarcoidosis

Louis E. Siltzbach, Associate Professor of Medicine, Columbia University College of Physicians and Surgeons, New York City

Tuberculous Effusions

C. James Duke, Clinical Instructor in Medicine, Georgetown University School of Medicine, Washington, D. C.

Other Tuberculous Processes

Howard A. Buechner, Chief, Medical Service, Veterans Administration Hospital, New Orleans, Louisiana

Fungal Infections

Donald B. Louria, Assistant Professor of Medicine, Cornell University Medical College, New York City

Poor-risk Thoracic Surgical Patients

W. Glenn Young, Jr., Associate Professor of Surgery, Duke University Medical Center, Durham, North Carolina

11:15 a. m.—*Aids in Chest Roentgenology*

Co-Chairmen: **Milton B. Kress,** Baltimore, Maryland, President Potomac Chapter, American College of Chest Physicians

John W. Trenis, Washington, D. C., Vice-President, Potomac Chapter, American College of Chest Physicians

Useful Radiographic Signs

Benjamin Felson, Professor and Director, Department of Radiology, University of Cincinnati College of Medicine, Cincinnati, Ohio

12:30 p. m. — ROUND TABLE LUNCHEON DISCUSSIONS

B-1 SKIN TESTS — THEIR VALUE AND VALIDITY

Michael L. Furcolow, Medical Director, U. S. Public Health Service; Associate Clinical Professor of Internal Medicine, University of Kansas School of Medicine, Kansas City, Kansas

Carroll E. Palmer, Chief of Operational Research, Tuberculosis Program, U. S. Public Health Service, Washington, D. C.

Louis E. Siltzbach, Associate Professor of Medicine, Columbia University College of Physicians and Surgeons, New York City

Moderator: **Capt. Robert O. Canada,** MC, Chief of Medicine, U. S. Naval Hospital, Bethesda, Maryland

B-2 AFTER THE X-RAY, WHAT NEXT?

Oscar Auerbach, Senior Medical Investigator, Veterans Administration Hospital, East Orange, New Jersey

Benjamin Felson, Professor and Director, Department of Radiology, University of Cincinnati College of Medicine, Cincinnati, Ohio

Donald L. Paulson, Clinical Associate Professor of Thoracic Surgery, University of Texas Southwestern Medical School, Dallas, Texas

Moderator: **Sol Katz,** Chief, Medical Service, Mt. Alto Veterans Administration Hospital, Washington, D. C.

B-3 FEASIBILITY OF PROSTHETIC REPLACEMENT OF THE MITRAL AND AORTIC VALVES

Charles A. Hufnagel, Professor of Surgery, Georgetown University School of Medicine, Washington, D. C.

Dean Warren, Associate Professor of Surgery, University of Virginia School of Medicine, Charlottesville, Virginia

Moderator: **Nina S. Braunwald,** Surgeon, National Heart Institute, Bethesda, Maryland

NOTE: Seating capacity at the round table luncheons is limited and reservations will be accepted in the order received. Please complete coupon on page 472.

Afternoon Session

1:55 p. m. — SCIENTIFIC SESSION

2:00 p. m.—Some Practical Considerations in Bronchial Carcinoma

Co-Chairmen: **Otto C. Brantigan,** Chief Surgeon, Church Home and Hospital, Baltimore, Maryland
William L. Cooke, Past-President, Potomac Chapter, Charleston, West Virginia

Unmasking the Many Disguises of Bronchial Carcinoma

Edgar W. Davis, Clinical Professor of Thoracic Surgery, Georgetown University School of Medicine, Washington, D. C.

How to Improve the Surgical Results in Bronchial Carcinoma

Donald L. Paulson, Clinical Associate Professor of Thoracic Surgery, University of Texas Southwestern Medical School, Dallas, Texas

How Strongly Does the Histologic Evidence Indict Smoking as a Cause of Bronchial Carcinoma?

Oscar Auerbach, Senior Medical Investigator, Veterans Administration Hospital, East Orange, New Jersey

How to Quit Smoking — And Why

George W. Ware, Clinical Instructor in Thoracic Surgery, Georgetown University School of Medicine, Washington, D. C.

3:30 p. m.—Symposium on Current Chemotherapeutic Issues

Co-Chairmen: **George R. Maxwell,** Assistant Professor of Medicine, West Virginia School of Medicine, Morgantown, West Virginia
Moe Weiss, Medical Director, Glenn Dale Hospital, Glenn Dale, Maryland

Management of Fulminating Staphylococcal Infections

Vernon Knight, Clinical Director, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland

Chemoprophylaxis of Tuberculosis

Julius L. Wilson, Director of Medical Education, American Thoracic Society, New York City

Management of Active Tuberculosis Resistant to the "Big Three" Drugs

Ross L. McLean, Associate Professor of Meedicine, Emory University School of Medicine, Atlanta, Georgia

Therapy of Atypical Acid-fast Infections

Daniel E. Jenkins, Professor of Medicine, Baylor University College of Medicine, Houston, Texas

Current Status of Amphotericin B in Fungal Infections

Michael L. Furcolow, Medical Director, U. S. Public Health Service; Associate Clinical Professor of Internal Medicine, University of Kansas School of Medicine, Kansas City, Kansas

Experience with a Promising New Antifungal Agent in 20 Patients with Systemic Mycoses

John P. Utz, Chief, Infectious Disease Service, Clinical Center, National Institutes of Health, Bethesda, Maryland

6:30 p. m. — BANQUET

8:00 p. m. — FIRESIDE CONFERENCES

Subjects and Discussion Leaders

1) **PITFALLS IN DIAGNOSIS OF RHEUMATIC FEVER AND RHEUMATIC HEART DISEASE**

Thomas E. Cone, Captain, MC, USN, Chief of Pediatrics, National Naval Medical Center, Bethesda, Maryland

Bernard J. Walsh, Associate Clinical Professor of Medicine, Georgetown University School of Medicine, Washington, D. C.

2) **MYOCARDIAL PROTECTION FOR PROLONGED BYPASS**

Dean Warren, Associate Professor of Surgery, University of Virginia School of Medicine, Charlottesville, Virginia

W. Glenn Young, Jr., Associate Professor of Surgery, Duke University, Medical Center, Durham, North Carolina

3) **NEWER ANTIBIOTICS**

Sol Katz, Chief, Medical Service, Mt. Alto Veterans Administration Hospital, Washington, D. C.

Vernon Knight, Clinical Director, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland

4) VIROLOGY AND THE CHEST PHYSICIAN

Robert Parrott, Medical Director, Children's Hospital, Washington, D. C.

John P. Utz, Chief, Infectious Disease Service, Clinical Center, National Institutes of Health, Bethesda, Maryland

5) ESOPHAGEAL PROBLEM CASES: TIPS IN DIAGNOSIS AND MANAGEMENT

Roy G. Klepser, Clinical Associate Professor of Thoracic Surgery, Georgetown University School of Medicine, Washington, D. C.

Arthur M. Olsen, Professor of Medicine, Mayo Foundation, Rochester, Minnesota

6) TRAUMATIC HEART DISEASE

Lt. Colonel Hu A. Blake, MC, Chief, Thoracic Surgery Service, Walter Reed General Hospital, Washington, D. C.

William C. Manion, Chief, Cardiovascular Surgery, Armed Forces Institute of Pathology, Washington, D. C.

Thomas W. Mattingly, Director of Medical Education, Washington Hospital Center, Washington, D. C.

7) LOWER LOBE TUBERCULOSIS

Jerome A. Gold, Assistant Professor of Medicine, State University of New York College of Medicine, Brooklyn, New York

Patrick B. Storey, Associate Professor of Medicine, University of Maryland School of Medicine, Baltimore, Maryland

8) SELECTION OF PATIENTS FOR EMPHYSEMA SURGERY

Otto C. Brantigan, Chief Surgeon, Church Home and Hospital, Baltimore, Maryland

James J. Feffer, Associate Clinical Professor of Medicine, George Washington School of Medicine, Washington, D. C.

Milton B. Kress, Instructor in Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland

9) GEOGRAPHY, ENVIRONMENT AND THE SYSTEMIC MYCOSES

Chester W. Emmons, Head, Medical Mycology Section, Laboratory of Infectious Diseases, National Institutes of Health, Bethesda, Maryland

Michael L. Furcolow, Medical Director, U. S. Public Health Service; Associate Clinical Professor of Internal Medicine, University of Kansas School of Medicine, Kansas City, Kansas

10) CLUES AND RED HERRINGS IN INTERPRETING CHEST X-RAY FILMS

Benjamin Felson, Professor and Director, Department of Radiology, University of Cincinnati College of Medicine, Cincinnati, Ohio

Forrest V. Schumacher, Chief, Department of Radiology, Washington Hospital Center, Washington, D. C.

NOTE: The Fireside Conferences are informal and offer an opportunity for free discussion. Discussion leaders will be seated at tables with proper identification. Physicians may participate in the discussion of their choice, or move on to other discussions when and if they desire.

MONDAY, NOVEMBER 28

Administrative Sessions

EXECUTIVE SESSIONS

10:00 a. m.—*Executive Council Meeting*

M. Jay Flipse, Miami, Florida, President

12:00 noon —*Luncheon*

Joint Meeting, Board of Governors and Board of Regents

Howell S. Randolph, Phoenix, Arizona, Chairman, Board of Governors

2:30 p. m.—*Semi-annual Meeting, Board of Regents*

Arthur M. Olsen, Rochester, Minnesota, Chairman

FOR RESERVATION FORM, PLEASE SEE PAGE 472

ADVANCE REGISTRATION AND RESERVATION FORM

AMERICAN COLLEGE OF CHEST PHYSICIANS
112 East Chestnut Street
Chicago 11, Illinois

Please find my enclosed check in the amount of $_____ for reservations at the following functions to be held at the Shoreham Hotel, in Washington, D. C., on Saturday and Sunday, November 26 and 27.

ROUND TABLE LUNCHEONS — Tickets: $4.00 each

Saturday, November 26 **Sunday, November 27**

First choice A— _____ B— _____

Second choice A— _____ B— _____

Please indicate choice by number as listed in the program

BANQUET (including cocktails) — Tickets: $8.50 each

Please reserve_____places at the dinner.

Applications for reservations at the Round Table Luncheons will be accepted in the order received. Your luncheon and dinner tickets will be available at the College Registration Desk, Shoreham Hotel, Washington, at the time you register.

Please make checks payable to the American College of Chest Physicians.

THERE IS NO REGISTRATION FEE

ALL PHYSICIANS ARE CORDIALLY INVITED TO ATTEND

Member_____ Non-member_____

NAME_____

ADDRESS_____

CITY/STATE_____

Accompanied by_____

Hotel_____

Arrival date_____ Departure date_____

Please return this form promptly.
Thank you.

For hotel reservations, please write directly to the Shoreham Hotel.